Impact 4.0

User Manual

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Contents

Document Conventions

In addition to the use of italics for names of documents, the font conventions that are used in this document are summarized in the table below.

Table 3.1.

Font	Example	Use
Sans serif	Project Table	Names of GUI features, such as panels, menus, menu items, buttons, and labels
Monospace	`$SCHRODINGER/maestro`	File names, directory names, commands, environment variables, and screen output
Italic	*filename*	Text that the user must replace with a value
Sans serif uppercase	CTRL+H	Keyboard keys

In descriptions of command syntax, the following UNIX conventions are used: braces { } enclose a choice of required items, square brackets [ ] enclose optional items, and the bar symbol | separates items in a list from which one item must be chosen. Lines of command syntax that wrap should be interpreted as a single command.

In this document, to *type* text means to type the required text in the specified location, and to *enter* text means to type the required text, then press the ENTER key.

References to literature sources are given in square brackets, like this: [10].

Introduction to Basic Impact

Impact is a molecular mechanics and dynamics program that provides the molecular mechanics component of Glide, Liaison, and QSite calculations. Some of the basic capabilities of Impact are also available from Maestro. These capabilities include molecular mechanics (MM) energy minimization, molecular dynamics (MD) simulations, hybrid Monte Carlo (HMC) simulations, and addition of explicit water solvent to a structure.

For information related to the installation and use of Impact, see the following documentation:

- The *Installation Guide*, which includes installation instructions for all Schrödinger products and documentation.
- The *Impact Command Reference Manual,* which contains syntax and keywords for Impact command input files.
- The *Maestro User Manual*, which describes how to use the features of Maestro, including the Atom Selection dialog box. An appendix describes command-line utilities, some of which may be used with Liaison.
- The *Maestro Command Reference Manual*, which contains commands, options, and arguments for running Maestro from the command line, including the Atom Specification Language (ASL) and the Entry Specification Language (ESL).

1.1 Citing Impact in Publications

The use of this product and its components should be acknowledged in publications as:

Impact, version 4.0, Schrödinger, LLC, New York, NY, 2005.

Introduction to Maestro

Maestro is the graphical user interface for all of Schrödinger's products: CombiGlide™, Epik™, Glide™, Impact™, Jaguar™, Liaison™, LigPrep™, MacroModel®, Phase™, Prime™, QikProp™, QSite™, SiteMap™, and Strike™. It contains tools for building, displaying, and manipulating chemical structures; for organizing, loading, and storing these structures and associated data; and for setting up, monitoring, and visualizing the results of calculations on these structures. This chapter provides a brief introduction to Maestro and some of its capabilities. For more information on any of the topics in this chapter, see the *Maestro User Manual*.

2.1 General Interface Behavior

Most Maestro panels are amodal: more than one panel can be open at a time, and a panel need not be closed for an action to be carried out. Each Maestro panel has a Close button so you can hide the panel from view.

Maestro supports the mouse functions common to many graphical user interfaces. The left button is used for choosing menu items, clicking buttons, and selecting objects by clicking or dragging. This button is also used for resizing and moving panels. The right button displays a shortcut menu. Other common mouse functions are supported, such as using the mouse in combination with the SHIFT or CTRL keys to select a range of items and select or deselect a single item without affecting other items.

In addition, the mouse buttons are used for special functions described later in this chapter. These functions assume that you have a three-button mouse. If you have a two-button mouse, ensure that it is configured for three-button mouse simulation (the middle mouse button is simulated by pressing or holding down both buttons simultaneously).

2.2 Starting Maestro

Before starting Maestro, you must first set the `SCHRODINGER` environment variable to point to the installation directory. To set this variable, enter the following command at a shell prompt:

csh/tcsh: `setenv SCHRODINGER` *installation-directory*

bash/ksh: `export SCHRODINGER=`*installation-directory*

You might also need to set the DISPLAY environment variable, if it is not set automatically when you log in. To determine if you need to set this variable, enter the command:

```
echo $DISPLAY
```

If the response is a blank line, set the variable by entering the following command:

csh/tcsh: `setenv DISPLAY` *display-machine-name*`:0.0`

bash/ksh: `export DISPLAY=`*display-machine-name*`:0.0`

After you set the SCHRODINGER and DISPLAY environment variables, you can start Maestro using the command:

```
$SCHRODINGER/maestro options
```

If you add the $SCHRODINGER directory to your path, you only need to enter the command maestro. Options for this command are given in Section 2.1 of the *Maestro User Manual*.

The directory from which you started Maestro is Maestro's current working directory, and all data files are written to and read from this directory unless otherwise specified (see Section 2.8 on page 25). You can change directories by entering the following command in the command input area (see page 6) of the main window:

```
cd directory-name
```

where *directory-name* is either a full path or a relative path.

2.3 The Maestro Main Window

The Maestro main window is shown in Figure 2.1 on page 5. The main window components are listed below.

The following components are always visible:

- **Title bar**—displays the Maestro version, the project name (if there is one) and the current working directory.
- **Auto-Help**—automatically displays context-sensitive help.
- **Menu bar**—provides access to panels.
- **Workspace**—displays molecular structures and other 3D graphical objects.

The following components can be displayed or hidden by choosing the component from the Display menu. Your choice of which main window components are displayed is persistent between Maestro sessions.

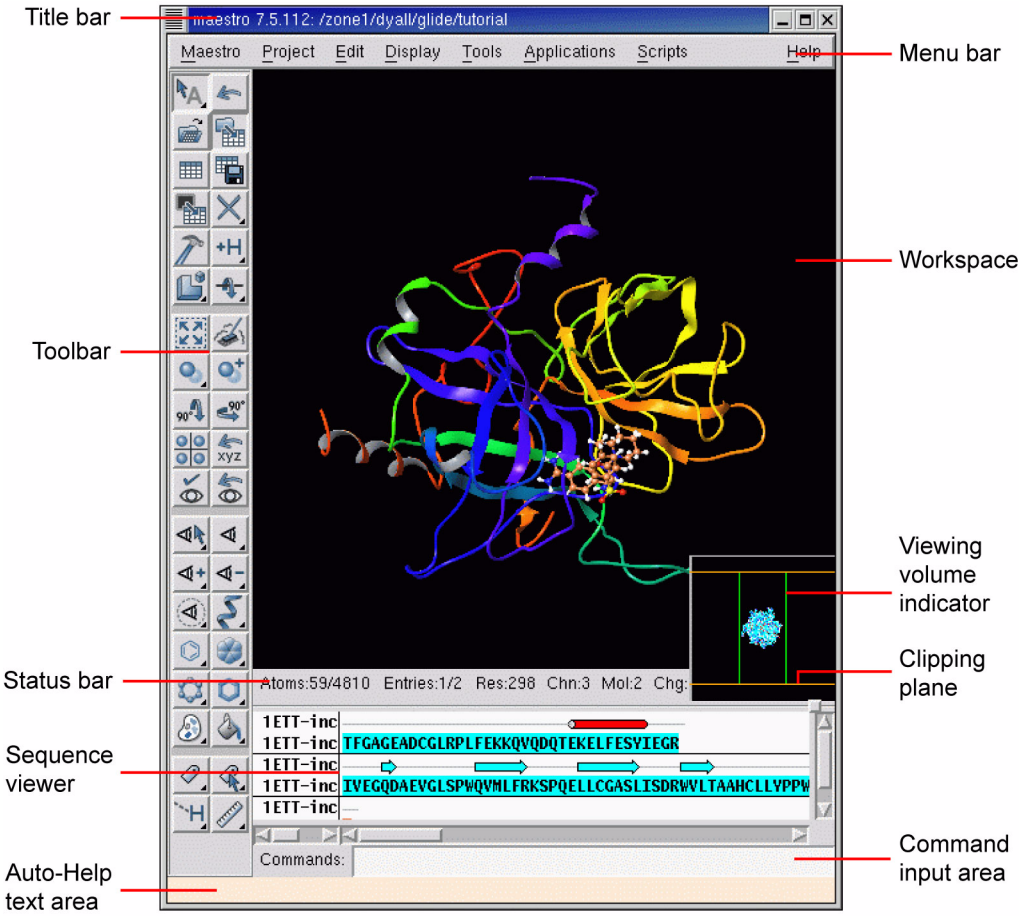

Figure 2.1. The Maestro main window.

- **Toolbar**—contains buttons for many common tasks and provides tools for displaying and manipulating structures, as well as organizing the Workspace.
- **Status bar**—displays information about a particular atom, or about structures in the Workspace, depending on where the pointer pauses (see Section 2.5 of the *Maestro User Manual* for details):
  - **Atom**—displays the chain, residue number, element, PDB atom name, formal charge, and title or entry name (this last field is set by choosing Preferences from the Maestro menu and selecting the Feedback tab).
  - **Workspace**—displays the number of atoms, entries, residues, chains, and molecules in the Workspace.

- **Clipping planes window**—displays a small, top view of the Workspace and shows the clipping planes and viewing volume indicators.
- **Sequence viewer**—shows the sequences for proteins displayed in the Workspace. See Section 2.6 of the *Maestro User Manual* for details.
- **Command input area**—provides a place to enter Maestro commands.

When a distinction between components in the main window and those in other panels is needed, the term *main* is applied to the main window components (e.g., main toolbar).

You can expand the Workspace to occupy the full screen, by pressing CTRL+=. All other components and panels are hidden. To return to the previous display, press CTRL+= again.

2.3.1 The Menu Bar

The menus on the main menu bar provide access to panels, allow you to execute commands, and control the appearance of the Workspace. The main menus are as follows:

- Maestro—save or print images in the Workspace, execute system commands, save or load a panel layout, set preferences, set up Maestro command aliases, and quit Maestro.
- Project—open and close projects, import and export structures, make a snapshot, and annotate a project. These actions can also be performed from the Project Table panel. For more information, see Section 2.4 on page 11.
- Edit—undo actions, build and modify structures, define command scripts and macros, and find atoms in the Workspace.
- Display—control the display of the contents of the Workspace, arrange panels, and display or hide main window components.
- Tools—group atoms; measure, align, and superimpose structures; and view and visualize data.
- Applications—set up, submit, and monitor jobs for Schrödinger's computational programs. Some products have a submenu from which you can choose the task to be performed.
- Scripts—manage and install Python scripts that come with the distribution and scripts that you create yourself. (See Chapter 13 of the *Maestro User Manual* for details.)
- Help—open the Help panel, the PDF documentation index, or information panels; run a demonstration; and display or hide Balloon Help (tooltips).

2.3.2 The Toolbar

The main toolbar contains three kinds of buttons for performing common tasks:

Action—Perform a simple task, like clearing the Workspace.

Display—Open or close a panel or open a dialog box, such as the Project Table panel.

Menu—Display a *button menu*. These buttons have a triangle in the lower right corner.

There are four types of items on button menus, and all four types can be on the same menu (see Figure 2.2):

- **Action**—Perform an action immediately.
- **Display**—Open a panel or dialog box.
- **Object types for selection**—Choose Atoms, Bonds, Residues, Chains, Molecules, or Entries, then click on an atom in the Workspace to perform the action on all the atoms in that structural unit.

  The object type is marked on the menu with a red diamond and the button is indented to indicate the action to be performed.
- **Other setting**—Set a state, choose an attribute, or choose a parameter and click on atoms in the Workspace to display or change that parameter.

The toolbar buttons are described below. Some descriptions refer to features not described in this chapter. See the *Maestro User Manual* for a fuller description of these features.

Figure 2.2. The Workspace selection ***button menu and the*** Adjust distances, angles or dihedrals ***button menu.***

Workspace selection
– Choose an object type for selecting
– Open the Atom Selection dialog box

Undo/Redo
Undo or redo the last action. Performs the same function as the Undo item on the Edit menu, and changes to an arrow pointing in the opposite direction when an Undo has been performed, indicating that its next action is Redo.

Open a project
Open the Open Project dialog box.

Import structures
Open the Import panel.

Open/Close Project Table
Open the Project Table panel or close it if it is open.

Save as
Open the Save Project As dialog box, to save the project with a new name.

Create entry from Workspace
Open a dialog box in which you can create an entry in the current project using the contents of the Workspace.

Delete
– Choose an object type for deletion
– Delete hydrogens and waters
– Open the Atom Selection dialog box
– Delete other items associated with the structures in the Workspace
– Click to select atoms to delete
– Double-click to delete all atoms

Open/Close Build panel
Open the Build panel or close it if it is open.

Add hydrogens
– Choose an object type for applying a hydrogen treatment
– Open the Atom Selection dialog box
– Click to select atoms to treat
– Double-click to apply to all atoms

Local transformation
– Choose an object type for transforming
– Click to select atoms to transform
– Open the Advanced Transformations panel

Adjust distances, angles or dihedrals
– Choose a parameter for adjusting
– Delete adjustments

Fit to screen
Scale the displayed structure to fit into the Workspace and reset the center of rotation.

Clear Workspace
Clear all atoms from the Workspace.

Set fog display state
Choose a fog state. Automatic means fog is on when there are more than 40 atoms in the Workspace, otherwise it is off.

Enhance depth cues
Optimize fogging and other depth cues based on what is in the Workspace.

Rotate around X axis by 90 degrees
Rotate the Workspace contents around the X axis by 90 degrees.

Rotate around Y axis by 90 degrees
Rotate the Workspace contents around the Y axis by 90 degrees.

Tile entries
Arrange entries in a rectangular grid in the Workspace.

Reset Workspace
Reset the rotation, translation, and zoom of the Workspace to the default state.

Save view
Save the current view of the Workspace: orientation, location, and zoom.

Restore view
Restore the last saved view of the Workspace: orientation, location, and zoom.

Display only selected atoms
– Choose an object type for displaying
– Click to select atoms to display
– Double-click to display all atoms

Display only
– Choose a predefined atom category
– Open the Atom Selection dialog box

Also display
– Choose a predefined atom category
– Open the Atom Selection dialog box

Undisplay
– Choose a predefined atom category
– Open the Atom Selection dialog box

Display residues within N angstroms of currently displayed atoms
– Choose a radius
– Open a dialog box to set a value

Show, hide, or color ribbons
– Choose to show or hide ribbons
– Choose a color scheme for coloring ribbons

Draw bonds in wire
– Choose an object type for drawing bonds in wire representation
– Open the Atom Selection dialog box
– Click to select atoms for representation
– Double-click to apply to all atoms

Draw atoms in CPK
– Choose an object type for drawing bonds in CPK representation
– Open the Atom Selection dialog box
– Click to select atoms for representation
– Double-click to apply to all atoms

Draw atoms in Ball & Stick
– Choose an object type for drawing bonds in Ball & Stick representation
– Open the Atom Selection dialog box
– Click to select atoms for representation
– Double-click to apply to all atoms

Draw bonds in tube
– Choose an object type for drawing bonds in tube representation
– Open the Atom Selection dialog box
– Click to select atoms for representation
– Double-click to apply to all atoms

Color all atoms by scheme
Choose a predefined color scheme.

Color residue by constant color
– Choose a color for applying to residues
– Click to select residues to color
– Double-click to color all atoms

Label atoms
– Choose a predefined label type
– Delete labels

Label picked atoms
– Choose an object type for labeling atoms
– Open the Atom Selection dialog box
– Open the Atom Labels panel at the Composition tab
– Delete labels
– Click to select atoms to label
– Double-click to label all atoms

Display H-bonds
– Choose bond type:
intra—displays H-bonds within the selected molecule
inter—displays H-bonds between the selected molecule and all other atoms.
– Delete H-bonds
– Click to select molecule

Measure distances, angles or dihedrals
– Choose a parameter for displaying measurements
– Delete measurements
– Click to select atoms for measurement

2.3.3 Mouse Functions in the Workspace

The left mouse button is used for selecting objects. You can either click on a single atom or bond, or you can drag to select multiple objects. The right mouse button opens shortcut menus, which are described in Section 2.7 of the *Maestro User Manual*.

The middle and right mouse buttons can be used on their own and in combination with the SHIFT and CTRL keys to perform common operations, such as rotating, translating, centering, adjusting, and zooming.

Table 2.1. Mapping of Workspace operations to mouse actions.

Mouse Button	Keyboard	Motion	Action
Left		click, drag	Select
Left	SHIFT	click, drag	Toggle the selection
Middle		drag	Rotate about X and Y axes Adjust bond, angle, or dihedral
Middle	SHIFT	drag vertically	Rotate about X axis
Middle	SHIFT	drag horizontally	Rotate about Y axis
Middle	CTRL	drag horizontally	Rotate about Z axis
Middle	SHIFT + CTRL	drag horizontally	Zoom
Right		click	Spot-center on selection
Right		click and hold	Display shortcut menu
Right		drag	Translate in the X-Y plane
Right	SHIFT	drag vertically	Translate along the X axis
Right	SHIFT	drag horizontally	Translate along the Y axis
Right	CTRL	drag horizontally	Translate along the Z axis
Middle & Right		drag horizontally	Zoom

2.3.4 Shortcut Key Combinations

Some frequently used operations have been assigned shortcut key combinations. The shortcuts available in the main window are described in Table 2.2.

Table 2.2. Shortcut keys in the Maestro main window.

Keys	Action	Equivalent Menu Choices
CTRL+B	Open Build panel	Edit > Build
CTRL+C	Create entry	Project > Create Entry From Workspace
CTRL+E	Open Command Script Editor panel	Edit > Command Script Editor
CTRL+F	Open Find Atoms panel	Edit > Find
CTRL+H	Open Help panel	Help > Help
CTRL+I	Open Import panel	Project > Import Structures
CTRL+M	Open Measurements panel	Tools > Measurements
CTRL+N	Create new project	Project > New
CTRL+O	Open project	Project > Open
CTRL+P	Print	Maestro > Print
CTRL+Q	Quit	Maestro > Quit
CTRL+S	Open Sets panel	Tools > Sets
CTRL+T	Open Project Table panel	Project > Show Table
CTRL+W	Close project	Project > Close
CTRL+Z	Undo/Redo last command	Edit > Undo/Redo
CTRL+=	Enter and exit full screen mode (Workspace occupies full screen)	None

2.4 Maestro Projects

All the work you do in Maestro is done within a *project*. A project consists of a set of *entries*, each of which contains one or more chemical structures and their associated data. In any Maestro session, there can be only one Maestro project open. If you do not specify a project when you start Maestro, a *scratch* project is created. You can work in a scratch project without saving it, but you must save it in order to use it in future sessions. When you save or close a project, all the view transformations (rotation, translation, and zoom) are saved with it. When you close a project, a new scratch project is automatically created.

Likewise, if there is no entry displayed in the Workspace, Maestro creates a *scratch* entry. Structures that you build in the Workspace constitute a scratch entry until you save the structures as project entries. The scratch entry is not saved with the project unless you explicitly add it to the project. However, you can use a scratch entry as input for some calculations.

To add a scratch entry to a project, do one of the following:

- Click the Create entry from Workspace button:

- Choose Create Entry from Workspace from the Project menu.
- Press CTRL+C.

In the dialog box, enter a name and a title for the entry. The entry name is used internally to identify the entry and can be modified by Maestro. The title can be set or changed by the user, but is not otherwise modified by Maestro.

Once an entry has been incorporated into the project, its structures and their data are represented by a row in the Project Table. Each row contains the row number, an icon indicating whether the entry is displayed in the Workspace (the In column), the entry title, a button to open the Surfaces panel if the entry has surfaces, the entry name, and any entry properties. The row number is not a property of the entry.

Entries can be collected into groups, and the members of the group can be displayed or hidden. Most additions of multiple entries to the Project Table are done as entry groups.

You can use entries as input for all of the computational programs—Glide, Impact, Jaguar, Liaison, LigPrep, MacroModel, Phase, Prime, QikProp, QSite, and Strike. You can select entries as input for the ePlayer, which displays the selected structures in sequence. You can also duplicate, combine, rename, and sort entries; create properties; import structures as entries; and export structures and properties from entries in various formats.

To open the Project Table panel, do one of the following:

- Click the Open/Close Project Table button on the toolbar

- Choose Show Table from the Project menu
- Press CTRL+T.

The Project Table panel contains a menu bar, a toolbar, and the table itself.

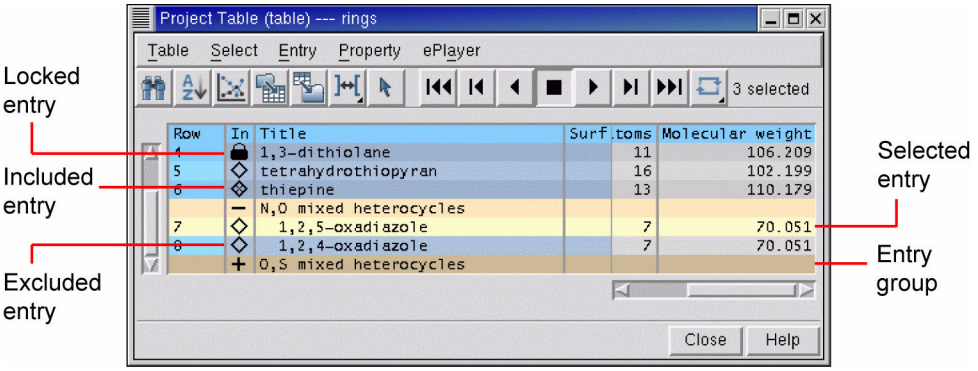

Figure 2.3. The** Project Table **panel.

2.4.1 The Project Table Toolbar

The Project Table toolbar contains two groups of buttons and a status display. The first set of buttons opens various panels that allow you to perform functions on the entries in the Project Table. The second set of buttons controls the ePlayer, which "plays through" the selected structures: each structure is displayed in the Workspace in sequence, at a given time interval. See Section 2.3.2 on page 7 for a description of the types of toolbar buttons. The buttons are described below.

Find
Open the Find panel for locating alphanumeric text in any column of the Project Table, except for the row number.

Sort
Open the Sort panel for sorting entries by up to three properties.

Plot
Open the Plot panel for plotting entry properties.

Import Structure
Open the Import panel for importing structures into the project.

Export Structure
Open the Export panel for exporting structures to a file.

Columns
Choose an option for adjusting the column widths.

Select only
Open the Entry Selection dialog box for selecting entries based on criteria for entry properties.

Go to start
Display the first selected structure.

Previous
Display the previous structure in the list of selected structures.

Play backward
Display the selected structures in sequence, moving toward the first.

Stop
Stop the ePlayer.

Play forward
Display the selected structures in sequence, moving toward the last.

Next
Display the next structure in the list of selected structures.

Go to end
Display the last selected structure.

Loop
Choose an option for repeating the display of the structures. Single Direction displays structures in a single direction, then repeats. Oscillate reverses direction each time the beginning or end of the list is reached.

The status display, to the right of the toolbar buttons, shows the number of selected entries. When you pause the cursor over the status display, the Balloon Help shows the total number of entries, the number shown in the table, the number selected, and the number included in the Workspace.

2.4.2 The Project Table Menus

- Table—find text, sort entries, plot properties, import and export structures, and configure the Project Table.
- Select—select all entries, none, invert your selection, or select classes of entries using the Entry Selection dialog box and the Filter panel.
- Entry—include or exclude entries from the Workspace, display or hide entries in the Project Table, and perform various operations on the selected entries.
- Property—display and manipulate entry properties in the Project Table.
- ePlayer—view entries in succession, stop, reverse, and set the ePlayer options.

2.4.3 Selecting Entries

Many operations in Maestro are performed on the entries selected in the Project Table. The Project Table functions much like any other table: select rows by clicking, shift-clicking, and control-clicking. However, because clicking in an editable cell of a selected row enters edit mode, you should click in the Row column to select entries. See Section 2.4.5 on page 16 for more information on mouse actions in the Project Table. There are shortcuts for selecting classes of entries on the Select menu.

In addition to selecting entries manually, you can select entries that meet a combination of conditions on their properties. Such combinations of conditions are called *filters*. Filters are Entry Selection Language (ESL) expressions and are evaluated at the time they are applied. For example, if you want to set up a Glide job that uses ligands with a low molecular weight (say, less than 300) and that has certain QikProp properties, you can set up a filter and use it to select entries for the job. If you save the filter, you can use it again on a different set of ligands that meet the same selection criteria.

To create a filter:

1. Do one of the following:
   - Choose Only, Add, or Deselect from the Select menu.
   - Click the Entry selection button on the toolbar.

   
2. In the Properties tab, select a property from the property list, then select a condition.
3. Combine this selection with the current filter by clicking Add, Subtract, or Intersect. These buttons perform the Boolean operations OR, AND NOT, and AND on the corresponding ESL expressions.
4. To save the filter for future use click Create Filter, enter a name, and click OK.
5. Click OK to apply the filter immediately.

2.4.4 Including Entries in the Workspace

In addition to selecting entries, you can also use the Project Table to control which entries are displayed in the Workspace. An entry that is displayed in the Workspace is *included* in the Workspace; likewise, an entry that is not displayed is *excluded*. Included entries are marked by an X in the diamond in the In column; excluded entries are marked by an empty diamond. Entry inclusion is completely independent of entry selection.

To include or exclude entries, click, shift-click, or control-click in the In column of the entries, or select entries and choose Include or Exclude from the Entry menu. Inclusion with the mouse works just like selection: when you include an entry by clicking, all other entries are excluded.

It is sometimes useful to keep one entry in the Workspace and include others one by one: for example, a receptor and a set of ligands. You can fix the receptor in the Workspace by selecting it in the Project Table and choosing Fix from the Entry menu or by pressing CTRL+F. A padlock icon replaces the diamond in the In column to denote a *fixed* entry. To remove a fixed entry from the Workspace, you must exclude it explicitly (CTRL+X). It is not affected by the inclusion or exclusion of other entries. Fixing an entry affects only its inclusion; you can still rotate, translate, or modify the structure.

2.4.5 Mouse Functions in the Project Table

The Project Table supports the standard use of shift-click and control-click to select objects. This behavior applies to the selection of entries and the inclusion of entries in the Workspace. You can also drag to resize rows and columns and to move rows.

You can drag a set of non-contiguous entries to reposition them in the Project Table. When you release the mouse button, the entries are placed after the first unselected entry that precedes the entry on which the cursor is resting. For example, if you select entries 2, 4, and 6, and release the mouse button on entry 3, these three entries are placed after entry 1, because entry 1 is the first unselected entry that precedes entry 3. To move entries to the top of the table, drag them above the top of the table; to move entries to the end of the table, drag them below the end of the table.

A summary of mouse functions in the Project Table is provided in Table 2.3.

Table 2.3. Mouse operations in the Project Table.

Task	Mouse Operation
Change a Boolean property value	Click repeatedly in a cell to cycle through the possible values (On, Off, Clear)
Display the Entry menu for an entry	Right-click anywhere in the entry. If the entry is not selected, it becomes the selected entry. If the entry is selected, the action is applied to all selected entries.
Display a version of the Property menu for a property	Right-click in the column header
Edit the text or the value in a table cell	Click in the cell and edit the text or value
Include an entry in the Workspace, exclude all others	Click the In column of the entry

Table 2.3. Mouse operations in the Project Table. (Continued)

Task	Mouse Operation
Move selected entries	Drag the entries
Paste text into a table cell	Middle-click
Resize rows or columns	Drag the boundary with the middle mouse button
Select an entry, deselect all others	For an unselected entry, click anywhere in the row except the In column; for a selected entry, click the row number.
Select or include multiple entries	Click the first entry then shift-click the last entry
Toggle the selection or inclusion state	Control-click the entry or the In column

2.4.6 Project Table Shortcut Keys

Some frequently used project operations have been assigned shortcut key combinations. The shortcuts, their functions, and their menu equivalents are listed in Table 2.4.

Table 2.4. Shortcut keys in the Project Table.

Keys	Action	Equivalent Menu Choices
CTRL+A	Select all entries	Select > All
CTRL+F	Fix entry in Workspace	Entry > Fix
CTRL+I	Open Import panel	Table > Import Structures
CTRL+N	Include only selected entries	Entry > Include Only
CTRL+U	Deselect all entries	Select > None
CTRL+X	Exclude selected entries	Entry > Exclude
CTRL+Z	Undo/Redo last command	Edit > Undo/Redo in main window

2.5 Building a Structure

After you start Maestro, the first task is usually to create or import a structure. You can open existing Maestro projects or import structures from other sources to obtain a structure, or you can build your own. To open the Build panel, do one of the following:

- Click the Open/Close Build panel button in the toolbar:

- Choose Build from the Edit menu.
- Press CTRL+B.

The Build panel allows you to create structures by drawing or placing atoms or fragments in the Workspace and connecting them into a larger structure, to adjust atom positions and bond orders, and to change atom properties. This panel contains a toolbar and three tabs.

2.5.1 Placing and Connecting Fragments

The Build panel provides several tools for creating structures in the Workspace. You can place and connect fragments, or you can draw a structure freehand.

To place a fragment in the Workspace:

1. Select Place.
2. Choose a fragment library from the Fragments menu.
3. Click a fragment.
4. Click in the Workspace where you want the fragment to be placed.

To connect fragments in the Workspace, do one of the following:

- Place another fragment and connect them using the Connect & Fuse panel, which you open from the Edit menu on the main menu bar or with the Display Connect & Fuse panel on the Build toolbar.

- Replace one or more atoms in the existing fragment with another fragment by selecting a fragment and clicking in the Workspace on the main atom to be replaced.
- Grow another fragment by selecting Grow in the Build panel and clicking the fragment you want to add in the Fragments tab.

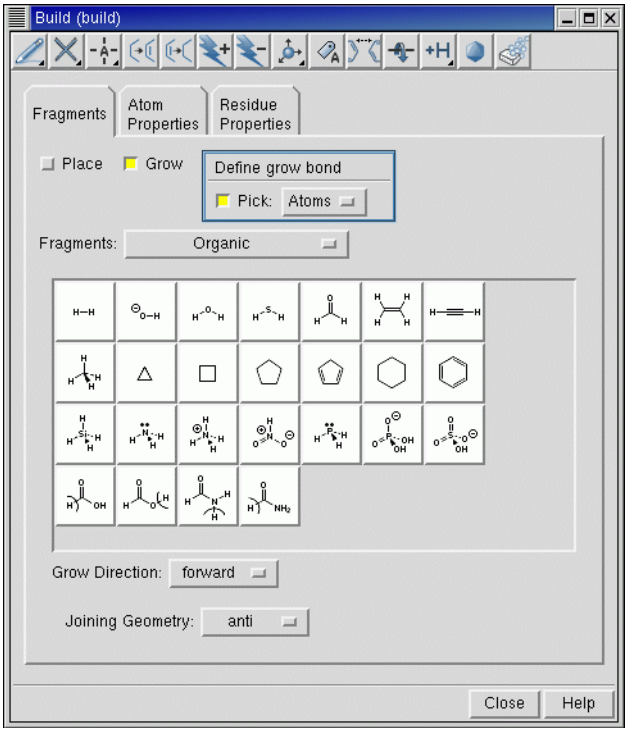

Figure 2.4. The* Build *panel.

Grow mode uses predefined rules to connect a fragment to the *grow bond*. The grow bond is marked by a green arrow. The new fragment replaces the atom at the head of the arrow on the grow bond and all atoms attached to it. To change the grow bond, choose Bonds from the Pick option menu in the Build panel and click on the desired grow bond in the Workspace. The arrow points to the atom nearest to where you clicked.

To draw a structure freehand:

1. Choose an element from the Draw button menu on the Build panel toolbar:

2. Click in the Workspace to place an atom of that element.
3. Click again to place another atom and connect it to the previous atom.
4. Continue this process until you have drawn the structure.
5. Click the active atom again to finish drawing.

2.5.2 Adjusting Properties

In the Atom Properties tab, you can change the properties of the atoms in the Workspace. For each item on the Property option menu—Element, Atom Type (MacroModel), Partial Charge, PDB Atom Name, Grow Name, and Atom Name—there is a set of tools you can use to change the atom properties. For example, the Element tools consist of a periodic table from which you can choose an element and select an atom to change it to an atom of the selected element.

Similarly, the Residue Properties tab provides tools for changing the properties of residues: the Residue Number, the Residue Name, and the Chain Name.

To adjust bond lengths, bond angles, dihedral angles, and chiralities during or after building a structure, use the Adjust distances, angles or dihedrals button on the main toolbar:

You can also open the Adjust panel from this button menu, from the Display Adjust panel button on the Build panel toolbar (which has the same appearance as the above button) or from the Edit menu in the main window.

2.5.3 The Build Panel Toolbar

The toolbar of the Build panel provides quick access to tools for drawing and modifying structures and labeling atoms. See Section 2.3.2 on page 7 for a description of the types of toolbar buttons. The toolbar buttons and their use are described below.

Free-hand drawing
Choose an element for drawing structures freehand in the Workspace (default C). Each click in the Workspace places an atom and connects it to the previous atom.

Delete
Choose an object for deleting. Same as the Delete button on the main toolbar, see page 8.

Set element
Choose an element for changing atoms in the Workspace (default C). Click an atom to change it to the selected element.

Increment bond order
Select a bond to increase its bond order by one, to a maximum of 3.

Decrement bond order
Select a bond to decrease its bond order by one, to a minimum of 0.

Increment formal charge
Select an atom to increase its formal charge by one.

Decrement formal charge
Select an atom to decrease its formal charge by one.

Move
Choose a direction for moving atoms, then click the atom to be moved. Moves in the XY plane are made by clicking the new location. Moves in the Z direction are made in 0.5 Å increments.

Label
Apply heteroatom labels as you build a structure. The label consists of the element name and formal charge, and is applied to atoms other than C and H.

Display Connect & Fuse panel
Open the Connect & Fuse panel so you can connect structures (create bonds between structures) or fuse structures (replace atoms of one structure with those of another).

Display Adjust panel
Open the Adjust panel so you can change bond lengths, bond angles, dihedral angles, or atom chiralities.

Add hydrogens
Choose an atom type for applying the current hydrogen treatment. Same as the Add hydrogens button on the main toolbar, see page 8.

Geometry Symmetrizer
Open the Geometry Symmetrizer panel for symmetrizing the geometry of the structure in the Workspace.

Geometry Cleanup
Clean up the geometry of the structure in the Workspace.

2.6 Selecting Atoms

Maestro has a powerful set of tools for selecting atoms in a structure: toolbar buttons, picking tools in panels, and the Atom Selection dialog box. These tools allow you to select atoms in two ways:

- Select atoms first and apply an action to them
- Choose an action first and then select atoms for that action

2.6.1 Toolbar Buttons

The small triangle in the lower right corner of a toolbar button indicates that the button contains a menu. Many of these buttons allow you to choose an object type for selecting: choose Atoms, Bonds, Residues, Chains, Molecules, or Entries, then click on an atom in the Workspace to perform the action on all the atoms in that structural unit.

For example, to select atoms with the Workspace selection toolbar button:

1. Choose Residues from the Workspace selection button menu:

   

   The button changes to:

   

2. Click on an atom in a residue in the Workspace to select all the atoms in that residue.

2.6.2 Picking Tools

The picking tools are embedded in each panel in which you need to select atoms to apply an operation. The picking tools in a panel can include one or more of the following:

- Pick option menu—Allows you to choose an object type. Depending on the operation to be performed, you can choose Atoms, Bonds, Residues, Chains, Molecules, or Entries, then click on an atom in the Workspace to perform the action on all the atoms in that structural unit.

  The Pick option menu varies from panel to panel, because not all object types are appropriate for a given operation. For example, some panels have only Atoms and Bonds in the Pick option menu.

- All button—Performs the action on all atoms in the Workspace.
- Selection button—Performs the action on any atoms already selected in the Workspace.
- Previous button—Performs the action on the most recent atom selection defined in the Atom Selection dialog box.
- Select button—Opens the Atom Selection dialog box.
- ASL text box—Allows you to type in an ASL expression for selecting atoms.

  ASL stands for Atom Specification Language, and is described in detail in the *Maestro Command Reference Manual*.

- Clear button—Clears the current selection

  

- Show markers option—Marks the selected atoms in the Workspace.

For example, to label atoms with the Label Atoms panel:

1. Choose Atom Labels from the Display menu.
2. In the Composition tab, select Element and Atom Number.
3. In the picking tools section at the top of the panel, you could do one of the following:
   - Click Selection to apply labels to the atoms already selected in the Workspace (from the previous example).
   - Choose Residues from the Pick option menu and click on an atom in a different residue to label all the atoms in that residue.

2.6.3 The Atom Selection Dialog Box

If you wish to select atoms based on more complex criteria, you can use the Atom Selection dialog box. To open this dialog box, choose Select from a button menu or click the Select button in a panel. See Section 5.3 of the *Maestro User Manual* for detailed instructions on how to use the Atom Selection dialog box.

2.7 Scripting in Maestro

Although you can perform nearly all Maestro-supported operations through menus and panels, you can also perform operations using Maestro commands, or compilations of these commands, called *scripts*. Scripts can be used to automate lengthy procedures or repetitive tasks and can be created in several ways. These are summarized below.

2.7.1 Python Scripts

Python is a full-featured scripting language that has been embedded in Maestro to extend its scripting facilities. The Python capabilities within Maestro include access to Maestro functionality for dealing with chemical structures, projects, and Maestro files.

The two main Python commands used in Maestro are:

- `pythonrun`—executes a Python module. (You can also use the alias `pyrun`.) The syntax is:

  `pythonrun` *module*`.`*function*

- `pythonimport`—rereads a Python file so that the next time you use the `pythonrun` command, it uses the updated version of the module. (You can also use the alias `pyimp`.)

From the Maestro Scripts menu you can install, manage, and run Python scripts. For more information on the Scripts menu, see Section 13.1 of the *Maestro User Manual*.

For more information on using Python with Maestro, see *Scripting with Python*.

2.7.2 Command Scripts

All Maestro commands are logged and displayed in the Command Script Editor panel. This means you can create a command script by performing the operations with the GUI controls, copying the logged commands from the Command History list into the Script text area of the panel, then saving the list of copied commands as a script.

To run an existing command script:

1. Open the Command Script Editor panel from the Edit menu in the main window.
2. Click Open Local and navigate to the directory containing the desired script.
3. Select a script in the Files list and click Open.

   The script is loaded into the Script window of the Command Script Editor panel.
4. Click Run Script.

Command scripts cannot be used for Prime operations.

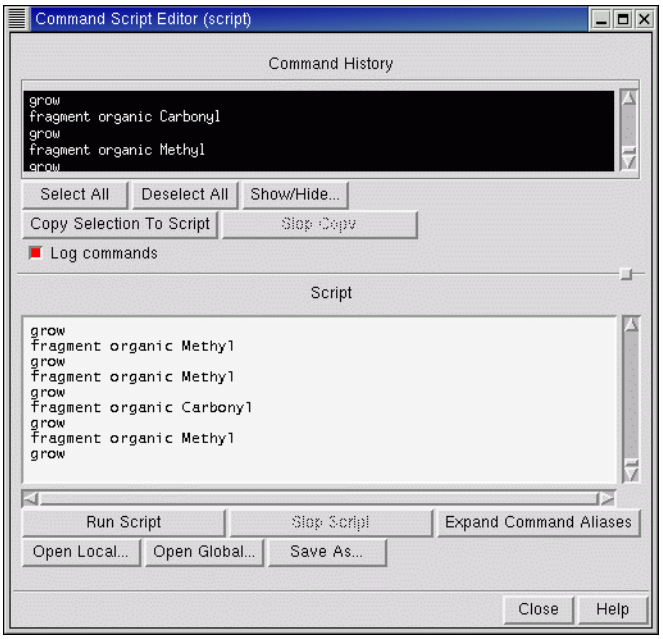

Figure 2.5. The Command Script Editor ***panel.***

2.7.3 Macros

There are two kinds of macros you can create: named macros and macros assigned to function keys F1 through F12.

To create and run a named macro:

1. Open the Macros panel from the Edit menu in the main window.
2. Click New, enter a name for the macro, and click OK.
3. In the Definition text box, type the commands for the macro.
4. Click Update to update the macro definition.
5. To run the macro, enter the following in the command input area in the main window:

   `macrorun` *macro-name*

   If the command input area is not visible, choose Command Input Area from the Display menu.

To create and run a function key macro:

1. Open the Function Key Macros panel from the Edit menu in the main window.
2. From the Macro Key option, select a function key (F1 through F12) to which to assign the macro.
3. In the text box, type the commands for the macro.
4. Click Run to test the macro or click Save to save it.
5. To run the macro from the main window, press the assigned function key.

For more information on macros, see Section 13.5 of the *Maestro User Manual*.

2.8 Specifying a Maestro Working Directory

When you use Maestro to launch Impact jobs, Maestro writes job output to the directory specified in the Directory tab of the Preferences panel. By default, this directory (the file I/O directory) is the directory from which you started Maestro.

To change the Maestro working directory:

1. Open the Preferences panel from the Maestro menu.
2. Click the Directory tab.
3. Select the directory you want to use for reading and writing files.

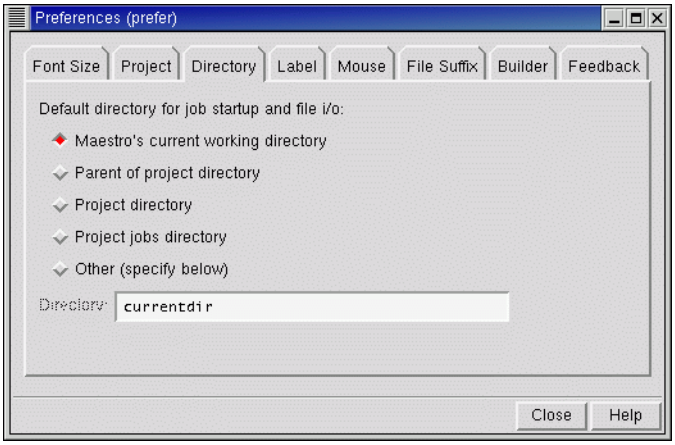

Figure 2.6. The** Directory **tab of the** Preferences **panel.

You can also set other preferences in the Preferences panel. See Section 12.2 of the *Maestro User Manual* for details.

2.9 Undoing an Operation

To undo a single operation, click the Undo button in the toolbar, choose Undo from the Edit menu, or press CTRL+Z. The word Undo in the menu is followed by text that describes the operation to undo. Not all operations can be undone: for example, global rotations and translations are not undoable operations. For such operations you can use the Save view and Restore view buttons in the toolbar, which save and restore a molecular orientation.

2.10 Running and Monitoring Jobs

Maestro has panels for each product for preparing and submitting jobs. To use these panels, choose the appropriate product and task from the Applications menu and its submenus. Set the appropriate options in the panel, then click Start to open the Start dialog box and set options for running the job. For a complete description of the Start dialog box associated with your computational program, see your product's User Manual. When you have finished setting the options, click Start to launch the job and open the Monitor panel.

The Monitor panel is the control panel for monitoring the progress of jobs and for pausing, resuming, or killing jobs. All jobs that belong to you can be displayed in the Monitor panel, whether or not they were started from Maestro. Subjobs are indented under their parent in the job list. The text pane shows output information from the monitored job, such as the contents

of the log file. The Monitor panel opens automatically when you start a job. If it is not open, you can open it by choosing Monitor from the Applications menu in the Maestro main window.

While jobs are running, the Detach, Pause, Resume, Stop, Kill, and Update buttons are active. When there are no jobs currently running, only the Monitor and Delete buttons are active. These buttons act on the selected job. By default, only jobs started from the current project are shown. To show other jobs, deselect Show jobs from current project only.

When a monitored job ends, the results are incorporated into the project according to the settings used to launch the job. If a job that is not currently being monitored ends, you can select it in the Monitor panel and click Monitor to incorporate the results. Monitored jobs are incorporated only if they are part of the current project. You can monitor jobs that are not part of the current project, but their results are not incorporated. To add their results to a project, you must open the project and import the results.

Further information on job control, including configuring your site, monitoring jobs, running jobs, and job incorporation, can be found in the *Job Control Guide* and the *Installation Guide*.

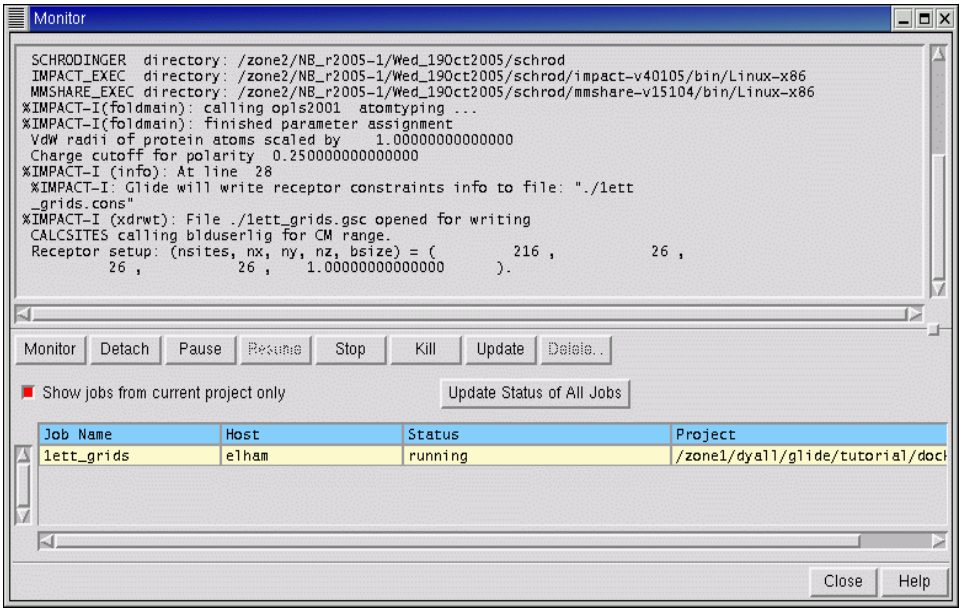

Figure 2.7. The* Monitor *panel.

2.11 Getting Help

Maestro comes with automatic, context-sensitive help (Auto-Help), Balloon Help (tooltips), an online help facility, and a user manual. To get help, follow the steps below:

- Check the Auto-Help text box at the bottom of the main window. If help is available for the task you are performing, it is automatically displayed there. It describes what actions are needed to perform the task.
- If your question concerns a GUI element, such as a button or option, there may be Balloon Help for the item. Pause the cursor over the element. If the Balloon Help does not appear, check that Show Balloon Help is selected in the Help menu of the main window. If there is Balloon Help for the element, it appears within a few seconds.
- If you do not find the help you need using either of the steps above, click the Help button in the lower right corner of the appropriate panel. The Help panel is displayed with a relevant help topic.
- For help with a concept or action not associated with a panel, open the Help panel from the Help menu or press CTRL+H.

If you do not find the information you need in the Maestro help system, check the following sources:

- The *Maestro User Manual*
- The Frequently Asked Questions page on the Schrödinger Support Center.

You can also contact Schrödinger by e-mail or phone for help:

- E-mail: help@schrodinger.com
- Phone: (503) 299-1150

2.12 Ending a Maestro Session

To end a Maestro session, choose Quit from the Maestro menu. To save a log file with a record of all operations performed in the current session, click Quit, save log file in the Quit panel. This information can be useful to Schrödinger support staff when responding to any problem you report.

Energy Minimization

3.1 Introduction to Basic Impact Applications

You can launch general-purpose Impact molecular mechanics calculations, called Basic Impact applications, from Maestro or from the command line, as described in Chapter 7. There are four Basic Impact applications:

- Energy Minimization
- Molecular Dynamics
- Hybrid Monte Carlo
- Soak

The common features of Impact panels and Impact Energy Minimization are described in this chapter; the other three applications are described in the chapters that follow.

For an extensive set of examples of input files for Basic Impact applications, see Appendix C of the *Impact Command Reference Manual*.

3.2 Common Features of Basic Impact Panels

Maestro panels for Basic Impact applications can be opened from the Impact submenu of the Applications menu. These panels have many common features. Some features described here appear in all panels; others are common to a subset of panels.

Controls that are specific to a panel appear in the middle section of the panel. Usually the controls will be contained in a series of tabs. Each tab contains settings relevant to the task that the panel performs.

3.2.1 Source of Structure Input

Use structures from

This option menu appears in all four Basic Impact panels. The options are:

Workspace (included entry)

This is the default option. The structure that is currently included in the Workspace is used as input to the job. This includes whatever atoms, molecules, or entries are part of the structure, even atoms that have been undisplayed. Calculations with Frozen or Constrained Atoms (see

the Constraints tab, Section 3.5 on page 39) requires that you use the Workspace structure to which the constraints have been applied.

Project Table (selected entry)

Select this option to use the entry that is currently selected in the Project Table. This may be different from the structure in the Workspace. Because atom constraints are applied to the Workspace structure, they are ignored if this option is chosen.

Input for Basic Impact jobs must be a single entry in the Project Table. To use a system consisting of two or more entries as the input, choose Merge from the Entry menu, create a combined entry, and run the job on that entry.

3.2.2 Common Buttons

In the lower part of most panels, the following buttons appear:

Start

Click the Start button to open the Start dialog box. Section 3.2.3 summarizes starting jobs using the Start dialog box.

Write

The Write button writes out all the files required for the job but does not actually start the job. Once the run files (an input file, *jobname*`.inp`, and one or more input structure files, *jobname_structure*`.mae`) are written by Maestro, the job can be run from the command line in a terminal window using the syntax:

```
$SCHRODINGER/impact -i jobname.inp
```

where *jobname*`.inp` is the input file for the job in question. The log output will be written to *jobname*`.log` by default; a different filename can be specified via `-o` *othername*`.log`.

Type `$SCHRODINGER/impact -h` for a usage summary of the `impact` command, or see Chapter 7 for a discussion of running Basic Impact applications from the command line.

Reset

Resets the options in all the tabs to the default values.

Close

The Close button, which is located on all Maestro panels, dismisses the current panel without starting the job or writing any files.

Help

The Help button opens the Help panel with an appropriate help topic displayed.

3.2.3 Starting Jobs

The features of the Start dialog box depend on the type of job which is being launched. The basic options include the following:

Output

The Start dialog box for Impact tasks includes an Output section containing one feature, the Incorporate option menu:

- Incorporate—Choose whether the new entries are appended to the Project Table, replace the existing entries, or are not incorporated into the Project Table at all.

Job

- Name—Type the name of the job in this text box, or accept the default name. When the job is started, the job name is used as the base name for files associated with the job. The Start dialog box for Impact jobs supplies an appropriate default name for each type of job (for example, `impact_soak`). However, a new default name is not automatically supplied each time you run a job of the same type. To avoid overwriting the job files from a job named `impact_soak`, use new names for the second and subsequent Soak jobs.

  Note: Impact does *not* automatically assign new names to jobs or files. If files of the same name exist, a warning is displayed before any files are overwritten.

- Host—Choose a host, if you want to run the job on a remote machine. This option menu displays all the hosts defined in the `$SCHRODINGER/schrodinger.hosts` file, with the number of processors on the host in parentheses. The default is `localhost`.
- Username—Enter your user name, if it is required for running the job on remote machines. The default value is the user name of the user who started Maestro. If this user name is not correct for the selected host, you can change it in this text box. If the job is running locally, this text box is ignored.
- CPUs—Specify the number of CPUs to use to run the job.

Once you have finished setting these options, you can click Start to start the job.

3.3 The Energy Minimization Panel

The Impact Energy Minimization panel is used to set up and run an Impact energy minimization calculation on the structure in the Workspace or on an entry selected in the Project Table.

Note: *Only one entry from the Maestro Project Table can be displayed and used for each minimization job.* If you need to minimize a system that spans two entries, use the Project Table's Merge option to create a combined entry, and use that as the basis for your simulation.

To open the Impact Energy Minimization panel, choose Minimization from the Impact submenu of the Applications menu in the main window.

The Energy Minimization panel has three tabs:

- Potential
- Constraints
- Minimization

All three tabs are described in detail in this chapter. The first two tabs also appear in the Maestro panels of two other Basic Impact applications: Molecular Dynamics Simulations and Hybrid MC Simulations.

3.4 The Potential Tab

The Potential tab sets parameters that control how Impact calculates the molecular-mechanics energy in a minimization calculation or dynamics simulation. This tab is included in the Impact Minimization, Impact Molecular Dynamics, and Impact Hybrid Monte Carlo panels. The options in the Potential tab are described below.

Force field option menu

The molecular-mechanics force field to use for the calculation is chosen from this menu. Only OPLS-AA force fields are available: the two options are

- OPLS_2001 (the default)
- OPLS_2003

For calculations that use Surface Generalized Born (SGB) continuum solvation, you may want to select the OPLS_2003 force field. With this force field, the improved parameterized nonpolar model (input file keyword `npsolv`) is used instead of the default SGB terms.

Electrostatic treatment

This option menu offers two methods for calculating the electrostatic component of the molecular mechanics energy:

- Constant dielectric

  This option calculates the electrostatic interaction between atoms *i* and *j* as:

  $$E_{ele} = 332.063762\ q_i q_j / (\varepsilon\ r_{ij})$$

  A constant dielectric is appropriate for a vacuum (gas-phase) calculation or when an explicit or implicit solvent model is used.

- Distance dependent dielectric

  This option calculates the electrostatic interaction between atoms *i* and *j* as:

  $$E_{ele} = 332.063762\ q_i q_j / \varepsilon\ r_{ij}^2$$

  A distance-dependent dielectric is sometimes used as a primitive model for the effect of solvent. In this model, the electrostatic interaction between a pair of atoms falls off rapidly as the distance between the atoms increases. However, continuum and explicit solvent models are much better at accounting for solvent effects than a distance-dependent dielectric.

The variables in the above formulae are defined as follows:

- E_{ele} is the electrostatic interaction in kcal/mol
- q_i and q_j are the partial atomic charges on atom *i* and *j*
- r_{ij} is the distance in Å between atoms *i* and *j*
- ε is the Dielectric constant (see below)

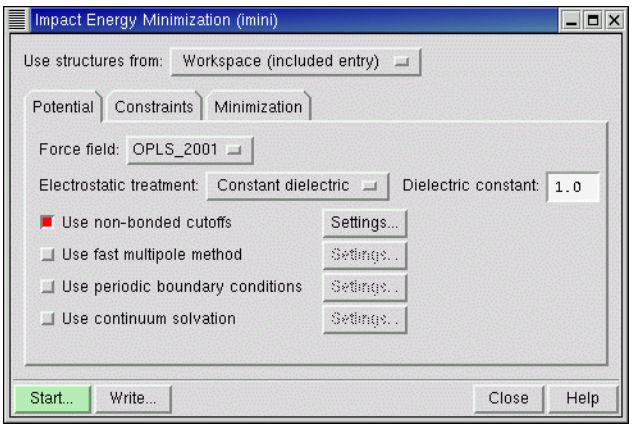

Figure 3.1. The Potential ***tab of the*** Impact Energy Minimization ***panel.***

Dielectric constant

This text box specifies the value of the dielectric constant ε used in the electrostatic calculations.

3.4.1 Potential Tab Methods

The lower part of the Potential tab allows you to choose among molecular mechanics treatments. When the check box for a method is selected, clicking the associated Settings button opens a panel of relevant options. The methods are listed briefly in this section, and then each Settings panel is described in more detail.

Use non-bonded cutoffs

In molecular-mechanics calculations it is often impractical to include the nonbonded (electrostatic and van der Waals) interactions between every pair of atoms. For large systems, many such pairs are separated by a great distance and contribute little to the interaction energy. Judicious truncation of the non-bonded interactions between widely separated pairs of atoms is an important strategy for reducing the resources needed for calculations on large systems.

When this option is selected, the associated Settings button can be used to open the Truncation panel, from which settings for non-bonded cutoffs can be specified. The default is to use non-bonded cutoffs.

Use fast multipole method

The Fast Multipole Method (FMM) is an algorithm for speeding up the electrostatic part of the molecular mechanics calculation for large systems. It is generally used for systems without periodic boundary conditions, where Ewald summation cannot be used, and for periodic boundary explicit solvent simulations with more than 20,000 atoms.

When this option is selected, the associated Settings button can be used to open the Fast Multipole Method panel, from which relevant settings can be specified.

Note: The Truncated Newton (TN) minimization method and the SGB and AGB continuum solvation methods are not available for use with the Fast Multipole Method.

Use periodic boundary conditions

Periodic boundary conditions are commonly used for calculations with explicit solvent, but can be employed for any periodic system.

When this option is selected, the associated Settings button can be used to open the Periodic Boundary Conditions panel, from which relevant settings can be specified.

Use continuum solvation

Three implicit solvent models, Surface Generalized Born (SGB), Analytic Generalized Born (AGB), and Poisson-Boltzmann (PBF) are available in Impact. (SGB is not available if FMM has been selected.) These methods account for the effects of solvent without the use of explicit water molecules. For details on these models, see the *Impact Command Reference Manual*.

When this option is selected, the associated Settings button can be used to open the Continuum Solvation panel, from which the choice of implicit solvation method and other settings relevant to continuum solvation can be specified.

3.4.2 The Truncation Panel

The Truncation panel defines the non-bonded cutoffs settings for an Impact calculation.

When sufficient care is taken, the use of non-bonded cutoffs to remove interactions between widely separated pairs of atoms is an important strategy for reducing the resources required to perform calculations on large systems. At present only residue-based cutoffs are supported for calculations set up in Maestro. This means that all atoms within complete residues that have any pair of atoms within the cutoff distance will be included in the non-bonded interaction list.

To open the Truncation panel, select Use non-bonded cutoffs and click the adjacent Settings button. The selection options in the Truncation panel are:

Update neighbor-list frequency (# steps) text box

When truncation is active, all the pairs that fall within the cutoff radius are stored in a "neighbor list". During a minimization calculation or dynamics simulation, the geometry of the structure may change so as to bring some pairs of atoms that were originally outside the cutoff distance to within the cutoff. Conversely, some pairs of atoms may move outside the cutoff distance. For these reasons, the neighbor list needs to be updated from time to time. The frequency of this update is controlled by this integer field. By default the neighbor list is updated every 10 minimization or dynamics steps. Increasing this value (updating the neighbor list *less* often) will speed up the calculation but may affect the accuracy of the results. Decreasing this value (updating the neighbor list *more* often) will slow down the calculation but may improve the accuracy.

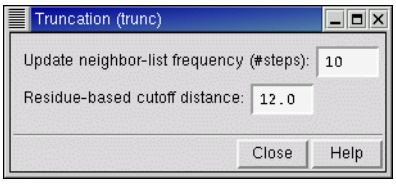

Figure 3.2. The** Truncation **panel.

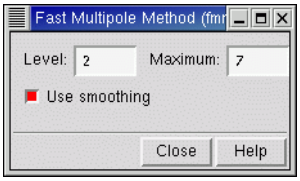

Figure 3.3. The Fast Multipole Method ***panel.***

Residue-based cutoff distance

This text box specifies the value for the cutoff distance. Increasing the cutoff distance will slow the calculation and require more memory, but may yield more accurate results. Decreasing the cutoff will speed up the calculation, but may reduce the accuracy of the results if significant non-bonded interactions are omitted. This is especially true for systems that include formally charged atoms, as such systems can have large long-range electrostatic interactions.

3.4.3 The Fast Multipole Method Panel

For large systems, the Fast Multipole Method (FMM) speeds the evaluation of the electrostatic and van der Waals parts of the molecular-mechanics energy by using interacting hierarchical multipoles to approximate the true electrostatic potential.

In systems where long-range electrostatic effects are important, the Fast Multipole Method or Ewald summation can be used to approximate these forces. For systems of fewer than 20,000 atoms, with explicit solvent and periodic boundary conditions, Ewald summation is typically used. At about 20,000 atoms, the Fast Multipole Method becomes faster than Ewald summation: FMM calculations scale linearly with the number of atoms N, while Ewald summation scales as N^2. FMM is also used for systems to which periodic boundary conditions cannot be applied, where Ewald summation cannot be used.

If the Fast Multipole Method is to be used with periodic boundary conditions:

- The simulation box must be a cube. Ensure that the Box [X,Y,Z] length values in the Periodic Boundary Conditions panel are equal.
- The system must be electrically neutral (the sum of all point charges must be zero).

The Fast Multipole Method cannot be used with the Truncated Newton minimization algorithm or with SGB continuum solvation.

To open the Fast Multipole Method panel, select Use fast multipole method and click the adjacent Settings button. The following options can be set:

Level

This text box sets the number of levels in the hierarchical tree used in the FMM calculation. This setting is relevant only when the reversible RESPA integrator is used with more than two inner stages. (See Section 4.2 on page 49.)

The Level parameter specifies the number of times the simulation box is divided into halves along each direction, a procedure known as octree decomposition. If a Level of 1 is set, one division is made along X, one along Y, and one along Z, so that the box is divided into 8 sub-cubes (octants). If Level=2 (the default), each sub-cube is further divided into 8 smaller cubes, for a total of 64, and so on. The value of Level should be at least 2: larger values yield increased accuracy at the cost of longer execution time, but may be useful in very large systems.

Maximum

This text box sets the maximum number of multipole moments to be used to approximate the potential and field produced by "far" clusters. Currently a minimum of 4 multipoles and a maximum of 20 multipoles are permitted; the default is 7.

Use smoothing

This option, selected by default, specifies the use of a smooth cutoff to separate into "near" and "far" components the forces that are computed explicitly from Coulomb's Law, rather than from the multipole expansions. This setting is relevant only when the reversible RESPA integrator is used with more than two inner stages. (See Section 4.2 on page 49.)

3.4.4 The Periodic Boundary Conditions Panel

Impact calculations can be performed with periodic boundary conditions. This technique is usually applied with explicit solvent in order to avoid nonphysical "edge effects." The system of interest is defined to be in a box of a given size, images of which are replicated throughout space to form an infinite 3D lattice.

The options in this panel allow you to set the size of the simulation box and to select and specify parameters for the Ewald summation method, which is used to efficiently sum long-distance electrostatic interactions in periodic systems. (This option cannot be used if you have selected Use fast multipole method.)

To open the Periodic Boundary Conditions panel, select Use periodic boundary conditions, then click the adjacent Settings button. The options of this panel are described below.

Box [X,Y,Z] lengths

Use these three text boxes to set the size of the simulation box. The minimum size for any dimension that Maestro will use is 18.62 Å, which is also the default in each dimension.

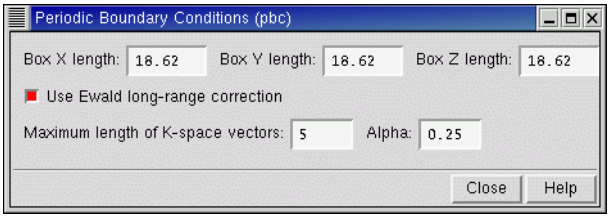

Figure 3.4. The Periodic Boundary Conditions ***panel.***

Use Ewald long-range correction

Click to select the Ewald summation method for efficiently summing long-distance electrostatic interactions in periodic systems. Unlike the Fast Multipole Method, Ewald summation does not require the net charge of the system to be zero. This setting is ignored when the Fast Multipole Method is used.

- Maximum length of K-space vectors

  If Use Ewald long-range correction is selected, you can use this text box to specify the number of component terms to retain in the reciprocal-space part of the summation. The default value is 5. Larger values yield increased accuracy but result in slower execution.

- Alpha

  If Use Ewald long-range correction is selected, you can use this text box to set the value of the a parameter. A reasonable value is 5.5/*L*, where *L* is the length of the cubic simulation box. The default value is 0.25.

3.4.5 The Continuum Solvation Panel

Impact supports three implicit solvent models, the Surface Generalized Born (SGB) model, the finite-element Poisson-Boltzmann Solver (PBF), and the Analytic Generalized Born (AGB) model. These methods simulate the effects of solvent without the use of explicit solvent molecules.

To open the Continuum Solvation panel, select Use continuum solvation and click the adjacent Settings button. The options of this panel are described below.

Solvation Method

From this option menu you can choose from the three continuum solvation models: Surface Generalized Born Model, Poisson Boltzmann Solver, and Analytic Generalized Born. If you use SGB solvation, you might want to select the OPLS_2003 force field in the Potential tab; the improved parameterized nonpolar model (input file keyword `npsolv`) will then be used instead of the default SGB terms.

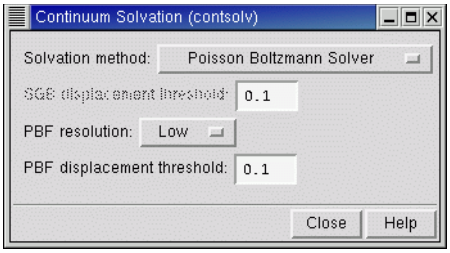

Figure 3.5. The** Continuum Solvation **panel.

SGB Displacement Threshold

When the Solvation method chosen is Surface Generalized Born Model, this text box specifies how far (in Å) any atom may move from the coordinates used in the previous SGB calculation before a new SGB calculation must be performed. If no atom has moved this distance, the previously calculated SGB energy and forces are used.

PBF Resolution

The Poisson-Boltzmann solver involves a finite-element calculation on a grid. The grid spacing controls both the accuracy of and time required for the PBF calculation. The default is to use a Low resolution grid, which should suffice for most protein work. If needed, greater accuracy can be achieved by setting this option menu to Medium or High.

PBF Displacement Threshold

This text box specifies how far (in Å) any atom may move from the coordinates used in the previous PBF calculation before a new PBF calculation must be performed. If no atom has moved this distance, the previously calculated PBF energy and forces are used.

3.5 The Constraints Tab

The Constraints tab of the Impact Energy Minimization panel is used to set up Impact *atom constraints.* These include constraints that freeze selected atoms at their input coordinates (frozen atoms) or keep them near their initial coordinates by applying a harmonic force (constrained atoms). Frozen atoms and constrained atoms can also be specified for Impact Molecular Dynamics (MD) and Impact Hybrid Monte Carlo (HMC) simulations, Liaison simulations, and QSite calculations, using the Constraints tabs in those panels.

The Constraints tabs in the Impact Dynamics and Impact Hybrid Monte Carlo panels can also be used to set up *bond constraints.* The MD and HMC simulations set up using these panels can use the SHAKE/RATTLE algorithm to constrain all bond lengths to ideal or reference values. Bond constraints are not available for Impact energy minimization calculations, and the

Constraints tab of the Impact Energy Minimization panel does not include bond constraint options; these options are described in Chapter 4.

In the Impact and Impact Energy Minimization panels, the Constraints tab contains only two buttons: the Frozen Atoms button and the Constrained Atoms button.

Frozen Atoms

Impact calculations can be performed with some atoms completely "frozen" so that they never move from their initial position during minimization or dynamics. Click this button to open the Frozen Atoms panel, in which you can select the atoms to be treated as frozen.

Constrained Atoms

Click this button to open the Constrained Atoms panel, in which you can select the atoms to be treated as "constrained". Constrained atoms are allowed to move, subject to harmonic penalty-function restraints that tether them elastically to their initial positions.

Note: The selection of atoms to be frozen or constrained applies only to the structure included in the Workspace when you make your selection. To apply the constraints, you must choose Workspace (included entry) as the source of structures (Use structures from option.)

3.5.1 The Frozen Atoms Panel

Use the Frozen Atoms panel to specify a set of atoms to be frozen during an Impact minimization calculation or dynamics simulation. Open the Frozen Atoms panel by clicking the Frozen Atoms button in the Impact Constraints tab.

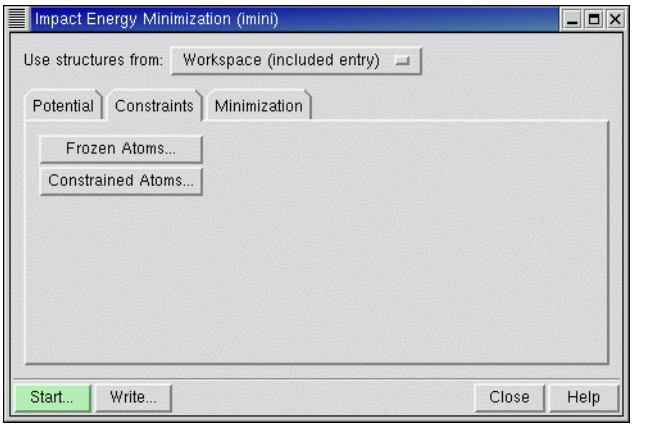

Figure 3.6. The** Constraints **tab of the** Impact Energy Minimization **panel.

The features of this panel are described below.

Frozen atoms list

The upper portion of the Frozen Atoms panel is a text area that lists the atom number of each atom that has been selected to be frozen.

Define frozen atoms

In this section you can specify atoms to be frozen using the standard picking controls: the Pick check box and menu, which is set to Atoms by default; the All button; and the Select button, which opens the Atom Selection dialog box. If you deselect the Pick check box, you can use the Workspace selection tool to select atoms, then click the Selection button to add those atoms to the list, or use the Previous button to return to the most recent selection.

Show markers option

This option is selected by default. The atoms to be frozen are marked with a red cross and a "padlock" icon in the Workspace display. To distinguish the currently selected frozen atom, Maestro colors the marker turquoise. Markers may be inconvenient if you are selecting large numbers of atoms. To prevent markers being added, or to remove the markers, deselect the option.

Delete

Click this button to remove the currently selected frozen atom from the frozen atoms list.

Delete All

Click this button to remove all currently defined frozen atoms from the frozen atoms list.

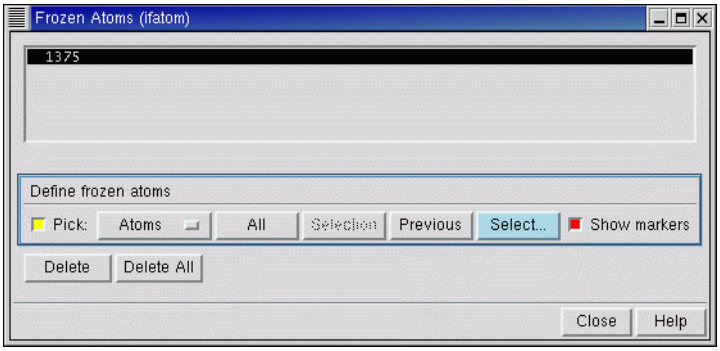

Figure 3.7. The Frozen Atoms ***panel.***

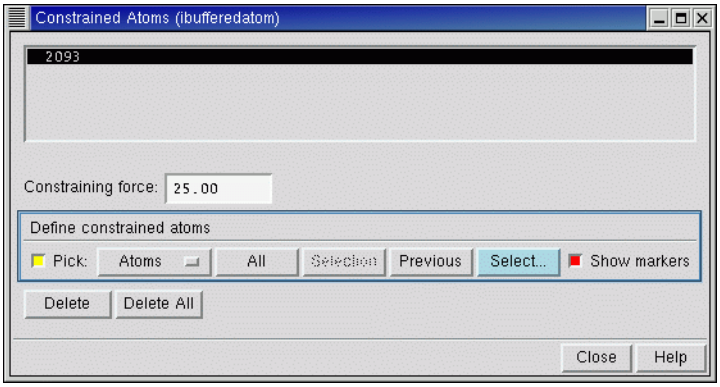

Figure 3.8. The Constrained Atoms ***panel.***

3.5.2 The Constrained Atoms Panel

You can use the Constrained Atoms panel to specify a set of atoms to be harmonically restrained during a molecular mechanics calculation. Such atoms are referred to as "constrained" atoms to distinguish them from "frozen" (completely fixed) atoms. To open the Constrained Atoms panel, click the Constrained Atoms button in the Constraints tab.

Constrained atoms list

The upper part of the Constrained Atoms list displays the list of atom numbers that have been selected to be constrained (restrained with a harmonic potential).

Constraining force

This text box sets the value of the harmonic force constant applied to the selected constrained atoms. The same force constant is used for all atoms. The default is 25.00 kcal/(Å^2 mol).

Define constrained atoms

In this section you can specify atoms to be constrained using the standard picking controls: the Pick check box and menu, which is set to Atoms by default; the All button; and the Select button, which opens the Atom Selection dialog box. If you deselect the Pick check box, you can use the Workspace selection tool to select atoms, then click the Selection button to add those atoms to the list, or use the Previous to return to the previous selection.

Show Markers

The Show markers option is selected by default. The atoms to be constrained are marked with a brown cross and a "spring" icon in the Workspace display. To distinguish the currently selected constrained atom, Maestro colors the marker turquoise. Markers may be inconvenient

if you are selecting large numbers of atoms. To prevent markers being added, or to remove the markers, deselect the option.

Delete

Click this button to remove the selected constrained atom from the constrained atoms list.

Delete All

Click this button to remove all defined constrained atoms from the constrained atoms list.

3.6 The Minimization Tab

The basic settings of the Impact energy minimization task are defined in the Minimization tab. You can use this tab to set options for an Impact energy minimization calculation on the structure specified in the Use structures from option menu in the Impact Energy Minimization panel. The Impact Minimization tab is available in the Impact Energy Minimization panel.

Note: In Liaison, minimization options for simulations are available in the Parameters tab.

The options available in this tab are described below.

Maximum minimization cycles

This text box sets the maximum number of cycles for the minimization calculation. The minimization terminates if it has not converged by this point. The default value of this setting is 100 iterations, but you can specify any value greater than or equal to zero. “Zero cycles” is a special case; it instructs Impact just to evaluate the energy for the current coordinates.

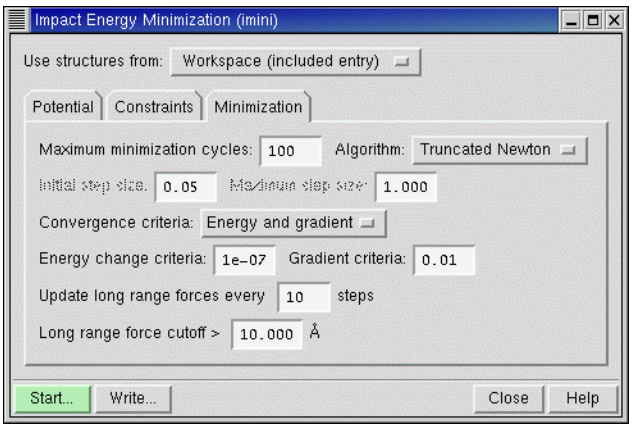

Figure 3.9. The Minimization ***tab of the*** Impact Energy Minimization ***panel.***

Algorithm

This option menu selects the minimization algorithm. The choices are:

- Truncated Newton (TN). This is a very efficient method for producing optimized structures and is the current default selection. A short conjugate gradient pre-minimization stage is performed first to help improve the convergence of the Truncated Newton algorithm.
    - The Truncated Newton minimization algorithm is not available if Use fast multipole method (FMM) has been selected in the Potential tab.
    - The Truncated Newton minimization algorithm is only available with the Surface Generalized Born (SGB) continuum solvation method. It is not available with explicit solvent models, such as set up in the Soak panel.
- Conjugate gradient. This is a good general optimization method.
- Steepest descent. This can be a good method for initiating a minimization on a starting geometry that contains large steric clashes. Convergence is very poor towards the end of minimization, where the conjugate gradient algorithm should be used.

Initial step size

This text box specifies the initial step size of the minimization cycle for conjugate gradient and steepest descent minimizations. The default value is 0.05 Å, but any positive value is allowed.

Maximum step size

This text box specifies the maximum step size of the minimization cycle for conjugate gradient and steepest descent minimizations. If the step size exceeds this value, the minimization will halt. The default value is 1.00 Å, but any positive value is allowed. The maximum step size is the maximum displacement allowed for an atom in any step of a minimization calculation.

Convergence criteria

This option menu sets the convergence criteria for the minimization. Either or both of two criteria—energy change and gradient—can be specified. Thus, the options are:

- Energy and Gradient. Choosing this option allows access to both the Energy change criteria and Gradient criteria text boxes.
- Energy change criteria. Use this text box to specify the value of the energy change criterion. The default value is 10^{-7} kcal/mol, but any positive value is allowed. The criterion is satisfied if two successive energies differ by less than the specified value.

- Gradient criteria. Use this text box to specify the value of the gradient criterion. The default value is 0.01 kcal/(mol∗Å), but any positive value is allowed. The criterion is satisfied if the norms of two successive gradients differ by less than the specified value.

Long-range forces options (for Truncated Newton minimizations):

- Update long range forces every *n* steps. Use this text box, when Truncated Newton minimization is selected, to specify the frequency with which long range forces are updated. Between these intervals, estimates of these forces are used. Every 10 steps is the default; smaller numbers (more frequent updates) can be used to improve convergence, but will make the optimization slower. Larger numbers for n may speed the calculation, but the maximum recommended value is 20.
- Long range force cutoff > *d* Angstroms. Use this text box, when Truncated Newton minimization is selected, to specify the distance beyond which forces are considered long range and are therefore updated every n steps. The default value is 10.000 Å.

Molecular Dynamics Simulations

You can use the Dynamics panel to set up and run a Molecular Dynamics (MD) simulation on the Workspace structure. Molecular Dynamics simulations examine stable, ground state molecules by applying Newton's equations of motion. The constant volume and temperature (NVT) ensemble is the default ensemble for MD simulations. The constant volume and energy (NVE) and constant pressure and temperature (NPT) ensembles are also supported.

NPT simulations require the use of periodic boundary conditions (see Section 3.4.4 on page 37). Such calculations often, but not always, use explicit solvent (see Chapter 6).

To open the Dynamics panel, choose Dynamics from the Impact submenu of the Maestro Applications menu. The Dynamics panel has four tabs:

- Potential
- Constraints
- MD Parameters
- Dynamics

The Potential and Constraints tabs are described in Chapter 3. The Constraints tab in the Dynamics panel includes features not available for energy minimization or Impact. These features are described here, along with the MD Parameters tab and the Dynamics tab.

When you have set the options in the Dynamics panel tabs to the desired value, click the Start button to open the Impact Dynamics - Start dialog box. The standard job start options are displayed, including the Incorporate option menu and the Job options: Name, Host machine, and Username (if different from the user name on the local host). For a description of these options, see Section 3.2.3 on page 31. The default job name for Impact Molecular Dynamics jobs is `impact_dyn`.

The input for an Impact Molecular Dynamics job can be either the contents of the Workspace or a single entry in the Project Table.

Note: *Only one entry from the Maestro Project Table can be displayed and used for each dynamics job.* If you need to merge two entries, use the Project Table's Merge option to create a combination entry, and use that as the basis for your simulation.

4.1 The Constraints Tab

In addition to the features described in Section 3.5 on page 39, the following features appear in the Constraints tab in the Impact Dynamics and HMC calculations:

Constrain all bonds

When this option is selected, all bond distances are constrained to their "ideal" values as defined by the molecular force field, using SHAKE to constrain the bond length and RATTLE to remove the relative motion (velocity) of the bonded atoms along the interatomic axis.

By default, Constrain all bonds is selected in the Impact Dynamics panel, but not selected in the Impact Hybrid Monte Carlo panel.

Make water molecules rigid

When this option is selected, the internal coordinates of water molecules are constrained to their "ideal" values as defined by the molecular force field. If you select Constrain all bonds, the HO distances are fixed but the HOH angles are not. This option adds the HH distances and the HO distances to the SHAKE distance constraints list, so that the water molecules become rigid. (The HO distances are not added if they are already in the list).

By default, Make water molecules rigid is selected in the Impact Dynamics panel, but not selected in the Impact Hybrid Monte Carlo panel.

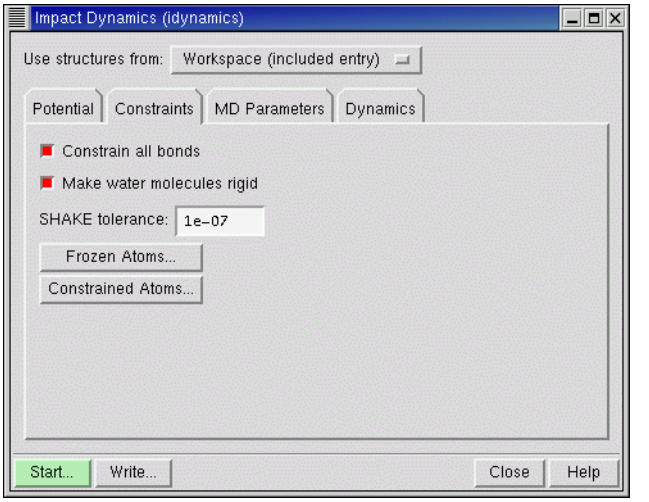

Figure 4.1. The Constraints ***tab of the*** Impact Dynamics ***panel.***

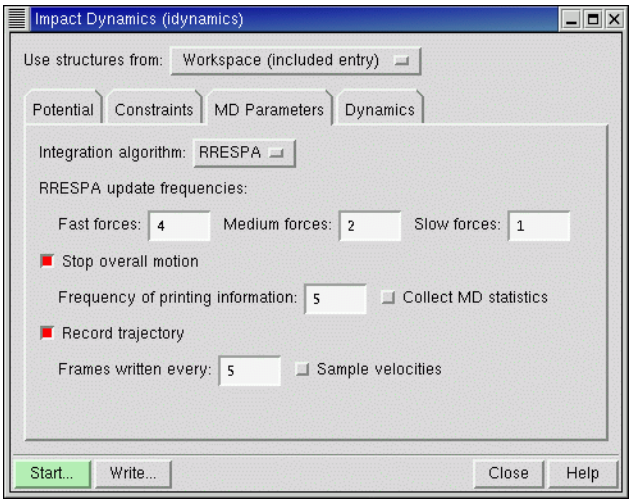

Figure 4.2. The** MD Parameters **tab of the** Impact Dynamics **panel.

SHAKE tolerance

This text box sets the tolerance for the SHAKE/RATTLE algorithm. The default value is 10^{-7} Å for SHAKE and 10^{-7} Å/ps for RATTLE. Increasing the tolerance will speed the calculation at the cost of allowing greater variation from the ideal values. Any value greater than zero is allowed. Note that the same numeric value is used for both tolerances, even though the units are different.

4.2 The MD Parameters Tab

In the MD Parameters tab you can specify molecular dynamics settings that affect both Molecular Dynamics (MD) and Hybrid Monte Carlo (HMC) calculations (see Chapter 5). The options are described below.

Integration algorithm

This option menu specifies the integration algorithm employed to integrate the Equations of Motion (EOM). The options are Verlet and RRESPA. There are no other settings to specify for the Verlet option. When RRESPA is selected, three other text boxes become active, as noted below.

- Verlet. The widely used velocity Verlet integration algorithm is the default for integrating the equations of motion in standard Cartesian-space molecular dynamics.

- RRESPA. The Reversible REference System Propagator Algorithm), the other choice offered by Impact for integrating the EOM, can be much more efficient. By breaking up the integration into large, medium, and small time steps (see the RRESPA update frequencies text boxes), this integrator devotes appropriate computational power to specific classes of forces—and thus keeps the calculation from being dominated by the small time steps needed to accurately integrate the fast motions (such as bond stretches). In particular, RRESPA integrates the fast motions with small time steps and the slow motions (far more numerous) with larger time steps.
- RRESPA update frequencies. If you select RRESPA, text boxes for Fast forces, Medium forces, and Slow forces are enabled.

  When the Fast Multipole Method (FMM) is also used, the forces are separated into three groups: those arising from well-separated bodies, those arising from first and second neighbors that are not very close, and those coming from the local expansions, which include bonded terms.

Table 4.1. RRESPA text boxes

Force	Interacting Species	Default Setting
Fast	Bonded and short-distance electrostatics	4
Medium	1^{st} and 2^{nd} neighbors that are not close	2
Slow	Long-distance non-bonded	1

All text boxes have acceptable ranges of any integer value greater than one. These entries modify the time step for the underlying MD or HMC simulation in the following way. Suppose that the global Time step specified in the Dynamics tab of the Impact Dynamics panel or the Hybrid MC tab of the Impact Hybrid Monte Carlo panel is δ. Then the time step used to integrate the slow forces is $\delta/1$, while the time step for medium forces is $\delta/(1 \times 2)$, and that for fast forces is $\delta/(1 \times 2 \times 4)$. Thus, the integration time step decreases as the product of the cumulative RRESPA update frequencies in going from slow to fast forces.

When FMM is not used (this is the more common case), only the Fast forces update frequency affects the calculation. In this case, the Medium and Slow forces are combined and use the global Time step set in the Dynamics tab of the Impact Dynamics panel or in the Hybrid MC tab of the Impact Hybrid Monte Carlo panel. Fast forces use the shorter time step computed by dividing the global Time step by the Fast forces update frequency.

Stop overall motion

When this option is selected (the default), overall rotational and translational motion (drift) of the system is subtracted from the calculation.

Frequency of printing information

This text box selects the frequency with which MD information is written during the simulation. The default is to print information every 5 MD steps. Any integer value greater than zero is allowed.

Collect MD statistics

This option is deselected by default. When it is selected, the MD statistics are collected and are written to the end of the Impact output file. These statistics measure fluctuations of the different energy terms.

Record trajectory

This option is deselected by default. When it is selected, trajectory information is written to the file *jobname*`.trj` in the Maestro working directory (or for Liaison, in the individual *ligandname* directories arrayed under the Liaison *jobname* directory). This information is written in binary format, but can be analyzed using the `ANALYSIS` task of Impact (which is not, however, supported by Maestro). A trajectory file contains a sequence of snapshots of the coordinates of the system and, if requested, of the velocities as well.

Note: The Impact analysis task must be run using Impact from the command line. See Chapter 7 for a brief overview of command-line Impact. See the *Impact Command Reference Manual* for additional information.

The following two options are applicable when Record trajectory has been selected:

Frames written every

This text box specifies how often trajectory information is written to the trajectory file. The default is every 5 MD steps. Any integer value greater than zero is allowed.

Sample velocities

This option is off by default. When it is selected, velocity information is written to the trajectory file.

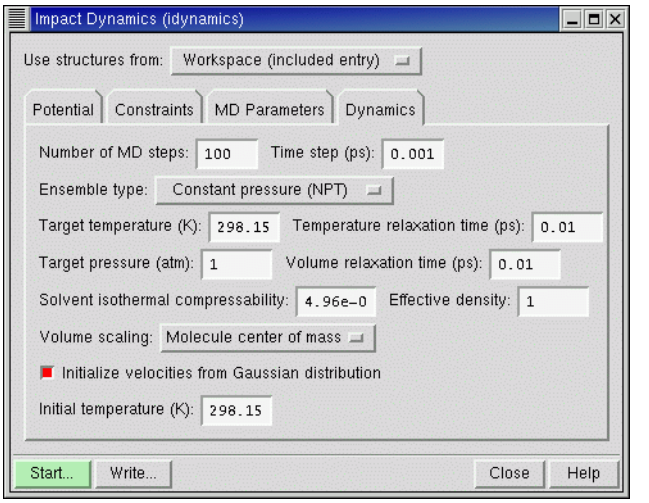

Figure 4.3. The** Dynamics **tab of the** Impact Dynamics **panel.

4.3 The Dynamics Tab

Use the Dynamics tab to choose the ensemble type, number of steps, time step, and other settings for a molecular dynamics calculation. The major options are described below. The other options in this tab are described under the major option to which they apply.

Number of MD steps

This text box sets the number of MD steps to be used for the simulation. The default setting is 100 steps, but any number greater than zero is allowed.

Time step

This text box sets the time step for the MD simulation. The default value is 0.001 ps, but any value greater than zero is allowed. A somewhat larger value (0.0015 or 0.002) may be suitable if bond lengths are constrained (see Section 4.1 on page 48) or if the RRESPA integrator is employed (see the MD Parameters tab in Section 4.2 on page 49).

Ensemble type

Impact offers three choices:

- Constant temperature (NVT)
- Constant energy (NVE)
- Constant pressure (NPT)

Depending on the ensemble chosen, various subsidiary settings become active.

Constant temperature (NVT) (the default)

With this ensemble type, volume and temperature are held constant during the simulation. This selection simulates coupling the system to an external heat bath (with a target temperature that is the same for all molecular species). Two settings become available when this ensemble type is chosen:

- Target temperature (K)—This text box sets the target temperature for an NVT or NPT simulation. The actual temperature will fluctuate about the specified value. At each MD step the velocities will be scaled so that the temperature will approach the desired value on a time scale determined by the Temperature relaxation time parameter. The default temperature is 298.15 K; the acceptable range is any value greater than or equal to 0 K.
- Temperature relaxation time (ps)—This text box sets the temperature relaxation time in picoseconds for velocity scaling. The default value is 0.01 ps; the acceptable range is any value greater than zero.

Constant energy (NVE)

With this ensemble, no temperature, volume, or pressure scaling is done. However, the total energy may not be conserved if nonbonded interaction cutoffs or too long an MD time step is used. In most cases, failure of energy conservation will lead to an unstable MD simulation. It is recommended that for this ensemble you deselect the nonbonded cutoffs option in the Potential tab, which is selected by default.

Constant pressure (NPT)

For this ensemble, both temperature and pressure are held constant during the simulation. This is accomplished by also coupling the system to a pressure bath using the algorithm of Berendsen et al. (*J. Chem. Phys*. **1984**, *81*, **3684**). Seven settings become available when this ensemble type is chosen. Along with Target temperature and Temperature relaxation time, described above, these are:

- Target pressure (atm)—This text box specifies the desired pressure in atmospheres. The actual pressure will fluctuate about the desired value. At each MD step the system will be scaled such that the pressure will approach the desired value on a time scale determined by the Volume relaxation time parameter. The default pressure value is 1 atm; the acceptable range is any positive or negative real value.
- Volume relaxation time (ps)—This text box sets the volume relaxation time in picoseconds for volume scaling in a constant pressure MD simulation. The default value is 0.01 ps; the acceptable range is any value greater than zero.

- Solvent isothermal compressibility—Isothermal compressibility or *k* (*1/V(dV/dP)*, in units of atm^{-1}) is the pressure analogue of the heat capacity and relates to the tendency of the solvent's volume to increase or decrease during pressure fluctuations in the system. The default is the value for water: $4.96x10^{-5}$ atm^{-1}; the acceptable range is any value greater than zero.
- Effective density—This text box specifies the effective density (g/cm^3) of solute molecules. This quantity is used to compute long-range corrections to the pressure during NPT molecular dynamics simulations. The default value is 1.0 g/cm^3; the acceptable range is any value greater than zero.
- Volume scaling

  Select one of two options for volume scaling in a MD simulation:

  - Molecule center of mass—This method of volume scaling, the default, is best for small molecules and is implemented by scaling the coordinates of the center of mass for each molecular species, relative to the center of the simulation box.
  - Atom based—This method of volume scaling is best for large molecules and is implemented by uniformly scaling all atomic coordinates relative to the center of the simulation box.

Initialize velocities from Gaussian distribution

When this option, available for all three ensembles, is selected, molecular velocities will be initialized as described, and the Initial temperature text box becomes available.

Initial temperature

When Initialize velocities from Gaussian distribution is selected, this text box specifies the initial temperature for the MD simulation. The default value is 298.15 K; the acceptable range is any value greater than or equal to 0 K.

Hybrid Monte Carlo Simulations

You can use the Hybrid Monte Carlo panel to set up and run a Hybrid Monte Carlo (HMC) simulation on the Workspace structure or on a selected entry in the Project Table. HMC simulations achieve relatively efficient sampling by interleaving Monte Carlo moves with a short sequence of molecular-dynamics steps. Because HMC is used mainly as a sampling method, for example, in Liaison binding affinity calculations, the MD steps can use a somewhat larger time step than would normally be advisable. The Metropolis algorithm determines which MD moves should be accepted or rejected. This ensures that the simulation will not go far astray, even if the MD time step would normally lead to a failure of energy conservation. This is why HMC is sometimes called "bad MD but good MC".

To open the Impact Hybrid Monte Carlo panel, choose Hybrid MC from the Impact submenu of the Maestro Applications menu.

The Impact Hybrid Monte Carlo panel has four tabs:

- Potential
- Constraints
- MD Parameters
- HybridMC

The Potential and Constraints tabs are described in Chapter 3. Additional features of the Constraints tab appear in Section 4.1 on page 48. Features of the MD Parameters tab relevant to both Impact Dynamics and Impact HMC are discussed in Section 4.2 on page 49. The HybridMC tab is discussed below.

When you have set the options in the Impact Hybrid Monte Carlo panel tabs to the desired value, click the Start button to open the Impact Hybrid Monte Carlo - Start dialog box. The standard job start options are displayed, including the Incorporate option menu and the Job options: Name, Host machine, and Username (if different from the username on the local host machine). For a description of these options, see Section 3.2.3 on page 31. The default job name for Impact Hybrid MC jobs is `impact_hmc`.

The input for an Impact Hybrid MC job can be either the contents of the Workspace or a single entry in the Project Table.

Note: *Only one entry from the Maestro Project Table can be displayed and used for each HMC job.* If you need to merge two entries, use the Project Table's Merge option to create a combination entry, and use that as the basis for your simulation.

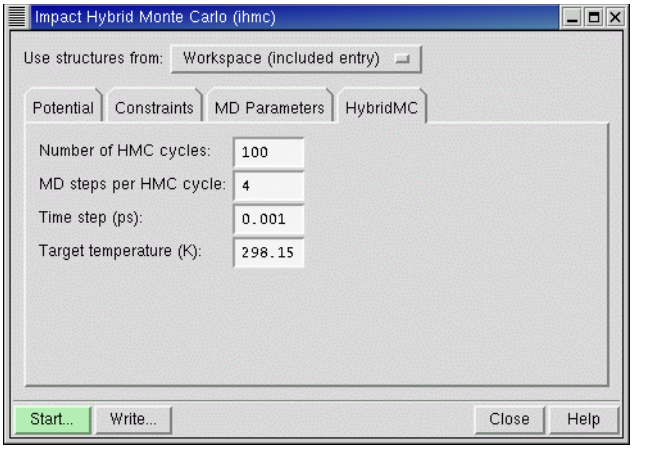

Figure 5.1. The HybridMC ***tab of the*** Impact Hybrid Monte Carlo ***panel.***

The HybridMC tab defines the basic settings of the HMC task for an Impact Hybrid Monte Carlo simulation. The selection options are:

Number of HMC cycles

The default number of HMC cycles is 100. The acceptable range is any number greater than zero.

MD steps per HMC cycle

The default number of MD steps per HMC cycle is 4. The acceptable range is any value greater than zero. Liaison simulations use 5 MD steps per HMC cycle.

Time step

This text box sets the MD global time step (in picoseconds) for the simulation. The default value is 0.001 ps. The acceptable range is any value greater than 0 ps. Because energy conservation is less important in HMC simulations, a time step of 0.002 ps or greater may be suitable.

Target temperature

This text box sets the target temperature (in Kelvin) for the HMC simulation. The default initial temperature is 298.15 K. The default target temperature is also 298.15 K. The acceptable range is any value greater than 0 K.

Soak—Add Explicit Water Solvent

Soak surrounds a structure with a box of solvent molecules. You can specify the box size and the solvent type and density. Then Impact adds the solvent molecules, removes any that are too close to the solute, and writes a Maestro-format file for the soaked system.

By default, Soak places 216 water molecules in the smallest permitted solvent box (at least 18.62 Å in each dimension.) The resulting box is not equilibrated due to edge effects. A short minimization is usually sufficient to obtain a fully equilibrated solvated system. It is recommended that constant temperature molecular dynamics, described in Chapter 4, be used for this and any other explicit solvent systems.

To model active sites or water shells around proteins with explicit solvent:

1. Run Soak.
2. Run a short minimization and constant temperature MD equilibration at room temperature.

You can set up a Soak job in the Soak panel. To open the Soak panel, choose Soak from the Impact submenu of the Maestro Applications menu.

When you have set the options in the Soak panel to the desired values, click Start, to open the Start dialog box. In this dialog box you can make job settings and start the job. The Incorporate option menu allows you to append the results to the Project Table or to leave them as a file, which is named *jobname*_out.mae. There is no option to replace existing entries. The default job name for Soak jobs is impact_soak. For a description of the Start dialog box options, see Section 4.2 of the *Job Control Guide*.

The input structure for a Soak job can be either the contents of the Workspace or a single entry in the Project Table.

The Soak panel has features common to Impact application panels, such as the Use structures from option menu and the Start, Write, Close, and Help buttons at the foot of the panel. For information on these common features, see Section 3.2 on page 29. The Soak panel also includes a single tab, labeled Soak, with the following options:

Solvent type

The solvent types available are SPC water (Simple Point Charge), TIP4P water, and TIP3P water.

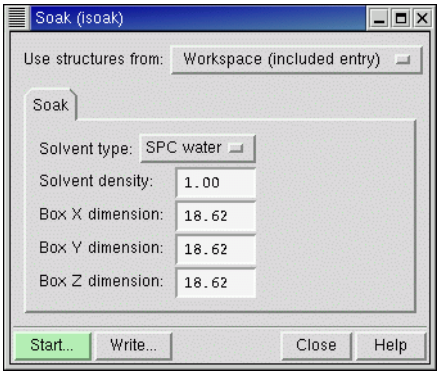

Figure 6.1. The* Soak *panel.

Solvent density

This text box specifies the density of solvent to be placed around the solute, in g/cm^3. The default is 1.00.

Box [X,Y,Z] dimensions

Use these three text boxes to specify the required size of the solvent box in angstroms. The minimum (and default) size for any dimension that Maestro will use is 18.62 Å. These values also update the size of the simulation box when periodic boundary conditions are applied. (See the discussion of periodic boundary conditions in Section 3.4.4 on page 37.)

Command-Line Impact

Although you will normally set up jobs using the controls and settings in the Maestro GUI, you can submit Impact jobs either from within Maestro or from the command line. Advantages of running from the command line include:

- The command-line scripts can run all full-featured jobs written using the Impact panels in Maestro, and also allow you to override specific run-time values that are not accessible through the Maestro interface.
- Command-line scripts allow you to run jobs when you want.
- Command-line scripts can be modified and jobs can be re-run without reconfiguring and reloading job settings in Maestro.
- Some job options, such as trajectory file analysis, are available only when you run Impact from the command line.

The `SCHRODINGER` environment variable must be set to run jobs. You can define `SCHRODINGER` as follows:

csh/tcsh: `setenv SCHRODINGER` *installation-directory*

bash/ksh: `export SCHRODINGER=`*installation-directory*

Unless otherwise specified, Schrödinger applications and utilities run under a job control system and are automatically run in the background. You need not add an `&` at the end of the commands to have them run and immediately return your command prompt. The `-WAIT` option of the `impact` command forces the shell to wait until the job is finished, so you can embed such commands in other scripts.

7.1 Running Impact From the Command Line

Basic Impact calculations can be run from the command line using the syntax shown below.

```
$SCHRODINGER/impact [options] [-i] input-file
```

To run `impact`, you must specify the input file, *input-file*. If *input-file* does not end in `.inp`, Impact looks first for *input-file* as specified. If that file doesn't exist, it then looks for *input-file*`.inp`. If `-i` is omitted, then *input-file* **must** end in `.inp` and must be the last argument in

the command line. If -i is included, the input file specification can be placed anywhere on the command line.

The options that you can specify when initiating jobs from the command line are described in Table 7.1 and Table 7.2. To view the usage summary information, define the SCHRODINGER environment variable and enter $SCHRODINGER/impact -h in a terminal window.

Table 7.1. Impact *command options*

Option	Description
-h	Print usage summary and exit
-v	Print version number of startup script and exit
-o *output-file*	File for writing output and log messages. If this option is omitted, Impact names the log file *jobname*.log, where *jobname* is taken from the Impact input file name.
-s *size*	Use specific "size" version of the Impact executable. Acceptable values for *size* are medium or huge. If omitted, medium is assumed in most cases; it is valid for up to 8000 atoms or 8000 bonds.

Table 7.2. Schrödinger job control options

Option	Description
-HOST *host* -HOST *host:n* -HOST "*host1 host2*"	Specify a remote machine (optionally, its number of processors *n*) on which to run an Impact job. Can also be used to specify a batch queue to submit the job to, or a collection of hosts for distributed or parallel jobs. Default is to run on the local host.
-USER *user*	Specify a remote user name to run Impact job under. Default is to use the local user name.
-WAIT	Do not return the command prompt until job finishes. This is useful in command scripts in which you have specified actions to take only after the Impact job finishes.
-WHICH	This switch is a diagnostic tool printing the available Impact installations you can use for the local machine. The job itself is not submitted. The first one listed is the default path; the options -REL, -VER, and -ARCH can direct your job to use a different installation.
-REL *release*	This option selects a specific version number of Impact to use. The default is the latest (highest number). Formats like -REL v4.0, -REL 35000, and -REL 27 are supported.

Table 7.2. Schrödinger job control options (Continued)

Option	Description
`-VER` *pattern*	If you have multiple installations installed, you can specify a pattern with the `-VER` option that matches the installation path to use for your job. The default installation is the one printed by `-WHICH`.
`-ARCH` *platform*	If you have more than one architecture installed for a given system, e.g., AIX-com and AIX-pwr3, then this flag can be used to select either of them, such as `-ARCH pwr3`.
`-LOCAL`	Force remote jobs to run in a local directory, rather than on the remote host. Only active when `-HOST` is used.

Note: The default molecular mechanics force field for Basic Impact applications is the OPLS2001 version of OPLS-AA. OPLS2003 is also available. OPLS2001 and OPLS2003 are designed to work with automatic atom-typing, and are incompatible with template mode. If you attempt to write a template file (Impact command `WRITE TEMPLATE`) while using OPLS2001, an error message is displayed to remind you that this command can only be used with OPLS1999 or OPLS2000 force fields. To use one of these older force fields, add a line to your input file before the `CREATE` task, for example:

```
SET FFIELD OPLS1999
```

For distributed processing, the `run_jobs.pl` script can be used. (Distributed processing for Basic Impact calculations is not available from the GUI.)

7.2 File Name Conventions

7.2.1 Location of Files and Working Directory

For Basic Impact applications, Maestro normally writes input files to the directory from which you launched Maestro (the *Maestro working directory*). Impact also normally writes its output files to the same location.

7.2.2 Impact File Names

A typical Impact job has one command-script file (*jobname*`.inp`), one or more structure files (*jobname*`.mae`, *jobname*`.pdb`, or *jobname*`.sdf`), and after execution, several output files (e.g., *jobname*`_out.mae` for structure files and *jobname*`.out` for textual data).

If a file already has the name of an output file, in many cases Impact renames the old file with a numerical extension (*filename*.out.01, *filename*.out.02, and so on) for archival purposes. The new job's output is then written to the base name (*filename*.out). If you do not need the old files, you can remove them.

Some files, such as *jobname*.log files, are newly written each time Impact runs a calculation. Likewise, old *jobname*_pv.mae files are overwritten. Other examples of files that are *not* incremented are:

- *jobname*_out.mae structure files, for Basic Impact minimization jobs.
- *jobname*_lig_min.mae and *jobname*_rec_min.mae files, for the minimization section in Liaison.
- *jobname*_rec_fin.mae and *jobname*_lig_fin.mae files, for the dynamics and HMC sampling methods in Liaison.

In addition, *jobname*_out.mae files are *not* produced by default for Liaison jobs—*jobname*_min.mae and/or *jobname*_fin.mae files are written instead.

Table 7.3 contains descriptions of the various file types. For more information, see the Maestro online help or the *Impact Command Reference Manual*.

Table 7.3. Liaison file extensions

Extension	Description
.inp	Impact input file or script. Impact input files are formatted plain-text files written in the Impact input file language, DICE. Maestro creates Impact input files before job submission, or you can create or edit them manually with a text editor.
.mae	A Maestro format structure file, a plain-text file written by Maestro containing atom, bond, and other information for one or more molecules.
.log	An Impact log file. If specified, a .log file captures standard output and standard error messages in text form. This file is overwritten during subsequent runs.
.out	An Impact output file containing information similar to that found in log files (no standard error). Output files are appended with numerical extensions when the input file is run again. Up to 99 output files are retained.
.01, .02, etc.	A file containing results from previous Impact calculations run from the corresponding *jobname*.inp file.
_out.mae	An Impact output structure file written in the Maestro file format. Liaison and some Impact jobs do not write *_out.mae output structure files.

7.3 Job Control

7.3.1 Overview

Once your jobs are launched, you can monitor their progress using the Monitor panel in Maestro. The command `$SCHRODINGER/jobcontrol` can also be used.

It has many options, which are summarized below. The two most useful options are:

```
$SCHRODINGER/jobcontrol -list
```

which will show the status of all your jobs, and:

```
$SCHRODINGER/jobcontrol -kill
```

to terminate any job and its subjobs, if any exist.

7.3.2 Usage Summary

The command format is:

`$SCHRODINGER/jobcontrol` *action* [*job_selection*]

where *action* is one of the following and *job_selection* specifies one or more jobs. The action will be applied to each selected job.

`-list`	List the JobId, job name and status. By default, lists all active jobs.
`-show`	Show basic information about the job
`-kill`	Terminate the job immediately
`-stop`	Terminate the job as soon as possible
`-pause`	Suspend the job temporarily
`-resume`	Continue running a paused job
`-monitor` *n*	Ask for monitoring files to be sent every *n* sec
`-cancel`	Cancel a job that has been launched, but not started
`-purge`	Remove completed job from the database
`-help`	Produce usage summary with query construction examples

The *job_selection* argument consists of one or more JobIds, job names, status codes, or queries. This field is optional; if *job_selection* is omitted, the default selection is the query `status!=completed`, that is, all active jobs. It can also be the word `all`, to select all jobs in the jobs database.

For more information, see the *Job Control Guide*. For an introduction to running and monitoring jobs in Maestro, see Section 2.10 on page 26.

7.3.3 Managing and Killing Impact Jobs

The job control facility may be used to manage and, if necessary, kill Impact jobs. This facility can be invoked from the Maestro Monitor panel. To kill a Impact job, select the *jobname*_sim entry and click the Kill button, and all the subjobs will quit as well.

For the purpose of killing Impact jobs, the `-list` or `-show` actions can be used to list the jobs in the jobs database, and `-kill` *jobname* or `-kill` *jobid* can then be used to kill one of these jobs. The top-level simulation script is called `simulate_`*jobname*. This script launches a job named *jobname*_sim. Use the *JobId* corresponding to this job as the argument to `jobcontrol -kill` *jobid*—all the individual ligand sub-jobs are killed as well. The job name *jobname*_sim can be substituted for the JobId in the `kill` command.

For more information on the job control facility, see the *Job Control Guide*.

Getting Help

Schrödinger software is distributed with documentation in PDF format. If the documentation is not installed in `$SCHRODINGER/docs` on a computer that you have access to, you should install it or ask your system administrator to install it.

For help installing and setting up licenses for Schrödinger software and installing documentation, see the *Installation Guide*. For information on running jobs, see the *Job Control Guide*.

Maestro has automatic, context-sensitive help (Auto-Help and Balloon Help, or tooltips), and an online help system. To get help, follow the steps below.

- Check the Auto-Help text box, which is located at the foot of the main window. If help is available for the task you are performing, it is automatically displayed there. Auto-Help contains a single line of information. For more detailed information, use the online help.
- If you want information about a GUI element, such as a button or option, there may be Balloon Help for the item. Pause the cursor over the element. If the Balloon Help does not appear, check that Show Balloon Help is selected in the Help menu of the main window. If there is Balloon Help for the element, it appears within a few seconds.
- For information about a panel or the tab that is displayed in a panel, click the Help button in the panel. The Help panel is opened and a relevant help topic is displayed.
- For other information in the online help, open the Help panel and locate the topic by searching or by category. You can open the Help panel by choosing Help from the Help menu on the main menu bar or by pressing CTRL+H.

If you do not find the information you need in the Maestro help system, check the following sources:

- *Maestro User Manual*, for detailed information on using Maestro
- *Maestro Tutorial*, for a tutorial on the basic features of Maestro
- *Maestro Command Reference Manual*, for information on Maestro commands
- *Job Control Guide*, for information on running jobs
- *Impact Command Reference Manual*, for Impact command syntax
- Frequently Asked Questions pages, at https://www.schrodinger.com/Impact_FAQ.html

The manuals are also available in PDF format from the Schrödinger Support Center. Information on additions and corrections to the manuals is available from this web page.

If you have questions that are not answered from any of the above sources, contact Schrödinger using the information below.

E-mail: help@schrodinger.com
USPS: Schrödinger, 101 SW Main Street, Suite 1300, Portland, OR 97204
Phone: (503) 299-1150
Fax: (503) 299-4532
WWW: http://www.schrodinger.com
FTP: ftp://ftp.schrodinger.com

Generally, e-mail correspondence is best because you can send machine output, if necessary. When sending e-mail messages, please include the following information, most of which can be obtained by entering `$SCHRODINGER/machid` at a command prompt:

- All relevant user input and machine output
- Impact purchaser (company, research institution, or individual)
- Primary Impact user
- Computer platform type
- Operating system with version number
- Impact version number
- Maestro version number
- mmshare version number

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